Guidelines for the Prevention and Treatment of Viral Hepatitis

October 2005

(Federal Bureau of Prisons - Clinical Practice Guidelines)

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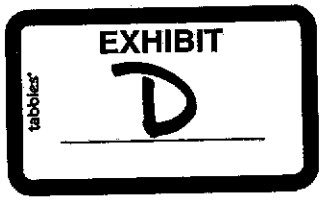

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What's New in the Document?

The following changes have been made since the February 2003 version of the guidelines:

Hepatitis A Virus (HAV)

- Incidence of new HAV infections at an historic low
- Reports of false positive IgM anti-HAV test results among persons with no recent history of acute hepatitis

Hepatitis B Virus (HBV)

- Decrease in incidence of acute HBV infections
- Greater emphasis on preventing infections through vaccination
- Update on treatment considerations for chronic hepatitis B
- Pegylated interferon and entecavir introduced as two new treatment options
- Update on management of persons with HIV/HBV co-infections
- Infection control emphasis on blood-glucose monitoring practices

Hepatitis C Virus (HCV)

- Update on treatment recommendations for acute hepatitis C
- RIBA testing no longer recommended for chronic HCV infection
- Screening for chronic HCV infection incorporated into baseline prevention visit
- New use of qualitative and quantitative HCV RNA tests
- Indications for liver biopsy broadened and "normal" ALT revisited
- Liver biopsy options for certain inmates with genotypes 2 or 3
- Abbreviated option of antiviral therapy for genotypes 2 or 3
- Reordering of hepatitis C treatment algorithm

Appendices

- Stepwise approach to managing chronic HBV infection deleted
- Contraindications to interferon and ribavirin updated
- Evaluation strategy for chronic hepatitis C updated and reordered
- Antiviral medication tables updated

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Appendices

1. Purpose

The Federal Bureau of Prisons Clinical Practice Guidelines for the Prevention and Treatment of Viral Hepatitis provide recommendations for the medical management of federal inmates with viral hepatitis infections or who are otherwise at risk of infection.

2. Hepatitis A Virus (HAV)

Transmission

HAV is transmitted fecal-orally and is acquired either by person-to-person contact or by the ingestion of contaminated food or water. Persons at increased risk of acquiring HAV infection include persons consuming contaminated food or water, men who have sex with other men, persons who inject illegal drugs, persons with clotting disorders who require clotting-factor concentrates, and close personal contacts of infected persons. Those persons newly infected with HAV are most contagious during the two weeks prior to the onset of jaundice. The presence of diarrhea increases contagiousness. HAV remains viable in the environment for weeks to months; therefore, transmission can readily occur through close personal contact such as by sexual exposure or sharing contaminated communal surfaces such as toilets.

The prevalence of previously acquired HAV infection among inmate populations is estimated at 22-39% and is largely determined by the risk-related behaviors of the inmate population and their community origin. American Indians, Alaskan Natives, and many persons from Latin America, Africa, the Middle East, China, and Southeast Asia come from communities with endemic HAV infection, where infection by early adulthood is commonplace.

In the United States, the incidence of new HAV infections is at an historic low, but clusters of hepatitis A cases continue to occur through community-based outbreaks. The highest rates of new HAV infections occur in the Western United States, and in large urban areas among men who have sex with men. Institutional outbreaks of hepatitis A are primarily limited to settings with children and have not involved correctional facilities.

Natural History

The mean incubation period from the time of infection with HAV until the onset of symptoms of acute hepatitis is 30 days (range: 15-50 days). Patients may present with jaundice, dark urine, nausea, diarrhea, and severe malaise. Acute hepatitis A is usually a self-limited illness, but a small number of patients develop fulminant hepatitis. Acute hepatitis eventually resolves with the development of natural, lifelong immunity.

Diagnosis

Acute hepatitis A is confirmed by a positive serum IgM anti-HAV titer that is detectable within 5-10 days after the onset of symptoms and persists up to 6 months after infection. All inmates presenting with symptoms of acute hepatitis should be tested for the presence of IgM anti-HAV, unless evidence of previous HAV infection exists (IgG anti-HAV-positive or total anti-HAV-positive/IgM anti-HAV-negative). False positive IgM anti-HAV test results have been reported among persons with no recent history of acute hepatitis. Therefore, positive IgM anti-HAV test results in inmates without clinical or laboratory evidence of acute hepatitis should be considered non-diagnostic.

Treatment

No effective antiviral therapies are available for acute hepatitis A. Therefore treatment efforts are largely supportive. Fulminant acute hepatitis A may be complicated by protracted nausea and vomiting, dehydration, high fever, impaired consciousness, and liver failure that requires intensive care hospitalization.

Prevention

Vaccine administration: Hepatitis A vaccine is an inactivated, highly immunogenic vaccine that is administered intramuscularly in the deltoid or gluteal (upper outer quadrant) muscle in a two-shot series, 6-12 months apart depending on the vaccine preparation. The two brands of hepatitis A vaccine (HAVRIX® formulated with a preservative; and VAQTA® formulated without a preservative) are equally effective and can be considered interchangeable. A bivalent combination vaccine, TWINRIX®, containing hepatitis A (HAVRIX®) and hepatitis B (ENGERIX-B®) antigens, is given on a 0, 1, 6-month schedule, and is equally effective. Vaccination of a person with previous immunity to HAV infection does not increase the risk of adverse events. Hepatitis A vaccine should not be administered to persons with hypersensitivity to alum or components of the vaccine. Prevaccination serologic screening for prior immunity to HAV infection by detecting IgG or total anti-HAV may be cost-effective for populations at high risk for previous HAV infection, such as certain Native American populations and foreign-born inmates from Latin America, Africa, Southeast Asia, and China, where HAV infection is endemic, as well as among inmates 50 years of age or older. Postvaccination serologic testing for immunity is not indicated since the hepatitis A vaccine is highly protective.

Vaccine indications: The following inmates should be considered candidates for hepatitis A vaccination:

- Inmates with liver disease or cirrhosis;
- Inmates with chronic HBV and HCV infections (priority should be given to inmates with underlying liver disease);

- Inmates with clotting-factor disorders who are administered clotting-factor concentrates (especially solvent-detergent-treated preparations);
- Users of injection and non-injection illegal drugs;
- Men who have sex with men; and
- Certain at-risk inmates in the context of a hepatitis A outbreak.

Hepatitis A vaccine is not routinely indicated for inmates workers who are plumbers or food workers.

Infection Control

Reporting: Each institution should have a surveillance system for notifiable infectious diseases in accordance with BOP policy. All cases of acute hepatitis A should be reported to state health authorities, as required by all the states and the Commonwealth of Puerto Rico. Acute hepatitis A cases should also be reported to the Central Office HSD in accordance with BOP policy.

Containment: Inmates diagnosed with acute hepatitis A should be considered contagious 3 weeks before to 10 days after the onset of jaundice for containment and contact investigation purposes. Inmates diagnosed with acute hepatitis A should be managed in accordance with the following guidelines:

- Isolated in a single cell with separate sink and toilet (e.g., observation cell) until 10 days after the onset of jaundice and until clinically improving without diarrhea;
- Immediately removed from any assigned duties as a food handler;
- Counseled regarding the importance of strict hand washing and other practical infection control measures;
- Managed using standard precautions to prevent fecal-oral transmission when in contact with contaminated body fluids, including wearing gloves or other personal protective equipment; and
- Evaluated by a health care provider daily while acutely ill for signs and symptoms of liver failure such as change in mental status, vomiting, and dehydration.

Contact investigations: A contact investigation, in consultation with local or state public health authorities, is required for all inmates with acute hepatitis A who were incarcerated during the incubation period, in order to enhance case-finding of other inmates who may be infected with HAV. All food handlers should be evaluated as part of the contact investigation. Public health officials should be directly involved in any potential foodborne outbreak to

determine the need for broad-based immunoprophylaxis. A contact investigation tool is attached in *Appendix 1a (Contact Investigation - Acute Hepatitis A)* and *Appendix 1b (Line Listing - Acute Hepatitis A)*.

Post-exposure management:

- **Indications:** The following susceptible contacts of an index case of hepatitis A are candidates for post-exposure prophylaxis with pooled serum immunoglobulin (IG):

  - cellmate(s)
  - sexual contacts
  - persons routinely sharing toilet facilities
  - very close contacts such as those who have shared eating utensils and cigarettes
  - co-worker food handlers (if source-case was a food handler).

More broad-based immunoprophylaxis of inmates and correctional staff may be indicated if the source-case was a food handler (in consultation with local and state health care authorities and the Central Office).

- **Administration:** Post-exposure prophylaxis is provided by passive immunization with pooled serum immunoglobulin (IG) in accordance with the following guidelines:

  - IG prophylaxis is not effective unless administered within 2 weeks of exposure.
  - Exposed inmates with previously documented natural immunity or hepatitis A vaccination do not require IG prophylaxis. If the inmate's immunity status to HAV infection is unknown, prophylaxis should be empirically administered.
  - Hepatitis A vaccination is not an effective post-exposure prophylaxis measure, but may be indicated for inmates at risk of future exposures in the context of an investigated outbreak.

3. Hepatitis B Virus (HBV)

Transmission

HBV is a bloodborne and sexually transmitted pathogen that is spread through percutaneous and mucosal exposures to infected blood and body fluids. Major modes of acquiring HBV infection include injection drug use, sexual intercourse with an infected partner, perinatal transmission from mother to child, chronic hemodialysis, and through certain occupational exposures. Tattooing with shared, contaminated needles or needle-like devices in jails and prisons is another potential mode of HBV transmission that specifically affects inmate populations. HBV is viable for at least 7 days on environmental surfaces and can be transmitted by sharing contaminated household items such as razors and toothbrushes. HBV is also transmitted perinatally or during childhood in parts of the world where the infection is

endemic and poorly controlled such as in Asia, the South Pacific, sub-Saharan Africa, and certain populations in the Arctic, South America, and the Middle East. Persons with chronic hepatitis B infection (HBsAg-positive) are often asymptomatic, but can still transmit their infection to others. Contagiousness increases significantly if persons with chronic HBV infection are also hepatitis B e antigen-positive (HBeAg-positive).

The incidence of acute hepatitis B is markedly declining in the United States, particularly among children and adolescents. At-risk adults, such as men who have sex with men and injection drug users, continue to be at risk for HBV infection and should be targeted for vaccination. Outbreaks of acute hepatitis B can occur within the correctional setting among unvaccinated inmates and may only be detected through careful contact investigations and laboratory surveillance.

Acute Hepatitis B Infection

Diagnosis and Natural History

The incubation period of HBV infection from transmission of infection until the onset of symptoms averages between 90-120 days (range: 45-180 days). Acute hepatitis B occurs in approximately 30-50% of infected adults and may be mild, severe, or fulminant. Signs and symptoms of acute hepatitis include fever, jaundice, nausea, abdominal pain, and malaise. Arthritis, serum sickness, and a nonspecific rash may also occur with acute HBV infection and, when present, are helpful diagnostically.

Acute HBV infection is confirmed by the serologic detection of IgM anti-HBc and HBsAg. The detection of HBsAg alone is not diagnostic for acute HBV infection, since persons with asymptomatic chronic HBV infection can be newly infected with other pathogens that cause acute hepatitis. IgM anti-HBc may persist at detectable levels for up to 2 years in a small subset of acutely infected persons.

Treatment

No effective therapies are available for acute hepatitis B, therefore treatment efforts are largely supportive. Fulminant disease, suggested by hemodynamic instability, dehydration, delirium, vomiting, and a rapidly receding liver edge, requires hospitalization and intensive management. Inmates with acute hepatitis B should be monitored during convalescence and thereafter to determine whether they develop chronic HBV infection (persistently HBsAg-positive) or clear their infection (anti-HBs-positive).

Chronic Hepatitis B Infection

Screening

Newly incarcerated inmates should be provided educational information on the transmission, natural history, and medical management of HBV infection by appropriately trained personnel in accordance with BOP policy. The BOP peer-oriented video on infectious diseases, the attached information in *Appendix 2 (Inmate Fact Sheet: Hepatitis B and C Viral Infections)*, and other appropriate patient educational tools should be used to facilitate counseling efforts.

Screening method: Screening for HBV infection should be performed by measuring HBsAg (additional HBV serologic tests may be warranted depending on the inmate's medical history).

Clinical indications: Inmates should be screened for hepatitis B regardless of sentencing status if any of the following clinical indications exist:

- Pregnant inmates (routine screening is medically imperative, regardless of previous screening results, due to the risk of perinatal transmission);
- Inmates on chronic hemodialysis who fail to develop antibodies after 2 series of vaccinations should be screened monthly (i.e., measure HBsAg);
- Asymptomatic inmates with elevated ALT levels of unknown etiology; and
- As clinically indicated (e.g., inmates with signs or symptoms of acute or chronic hepatitis, or percutaneous blood exposure, while incarcerated).

Non-sentenced inmates: In the absence of clinical indications, screening for HBV infection is generally not indicated for non-sentenced inmates. Asymptomatic non-sentenced inmates in BOP detention facilities with histories of injection drug use or other high-risk behaviors for HBV infection should be counseled regarding their risk of acquiring HBV infection and the behaviors that will reduce transmission of HBV infection to themselves and others during incarceration and upon release. Referrals to community testing sites should be made when appropriate. Long-term inmates in BOP detention facilities should be screened for HBV infection in accordance with guidelines for sentenced inmates.

Sentenced inmates: The following sentenced inmates should be screened for HBV infection within 6-12 months of incarceration at the prevention baseline visit:

- Inmates who have ever injected illegal drugs or shared equipment;
- Inmates who have received tattoos or body piercings while in jail or prison;
- Male inmates who have had sex with another man;

- Inmates with a history of chlamydia, gonorrhea, or syphilis;
- Inmates with HIV infection or HCV infection;
- Inmates from high-risk countries (i.e., Africa, Eastern Europe, Western Pacific, Asia, with the exception of Japan); and
- Inmates with a history of percutaneous exposure to blood.

Sentenced inmates who have risk factors for chronic HBV infection, but who initially refuse testing, should be counseled periodically regarding the need for testing during periodic prevention visits.

Diagnosis and Counseling

Diagnosis: The diagnosis of chronic HBV infection is confirmed by the serologic detection of hepatitis B surface antigen (HBsAg) on two separate occasions, 6 months apart; or the one-time detection of HBsAg, if total anti-HBc-positive/IgM anti-HBc-negative.

A complicated array of HBV serologic markers are useful, alone or in combination, in characterizing various phases of HBV infection. Serologic markers are outlined in *Appendix 3 (Interpretation of Hepatitis B Virus Serologic Markers)*.

Patient counseling: Inmates diagnosed with chronic HBV infection should be counseled by a health care provider about the natural history of the infection, potential treatment options, and specific measures for preventing transmission of HBV infection to others (during incarceration and upon release), including the following information and recommendations:

- Most persons with HBV infection will remain healthy, but a small number of persons will develop serious liver disease. Talk to your health care provider about your personal health status.
- Drug treatment options for chronic hepatitis B are developing. Medications may or may not be appropriate for you at this time. Talk to your doctor about your specific treatment plan.
- Do not shoot drugs, have sex with other inmates, or get a tattoo or body piercing while in prison.
- Do not share personal items that might have your blood on them, such as toothbrushes, dental appliances, nail-grooming equipment, or razors.
- Cover your cuts and skin sores to keep your blood from contacting other persons.
- Before release, talk to a health care provider about specific ways you can reduce the risk of transmitting HBV infection to others after you are released.

- Upon release, markedly limit alcohol consumption or abstain altogether, and speak to a physician prior to taking any new medications, including over-the-counter drugs such as nonsteroidal anti-inflammatory agents and herbal remedies, that may damage your liver.

- Upon release, do not donate blood, body organs, other tissue, or semen.

- Upon release, seek medical attention so that your condition is appropriately monitored and treated.

Natural History

The majority of adults acutely infected with HBV eventually clear HBsAg from the blood and develop antibodies to HBsAg (anti-HBs) that confer long-term protection from re-infection. A subset of persons acutely infected with HBV develop chronic HBV infection (HBsAg-positive for 6 months or longer). The risk of chronic HBV infection is much greater for persons from parts of the world where HBV is endemic and acquired perinatally, such as in Asia (with the exception of Japan). Immunosuppressed individuals are also more likely to develop chronic HBV infection.

Chronic hepatitis B infection disease course: Chronic HBV infection (HBsAg-positive) may result in chronic hepatitis or asymptomatic chronic infection, or eventually resolve.

- **Chronic hepatitis B** is diagnosed by the following four criteria:

  1) HBsAg-positive for > 6 months;
  2) serum HBV DNA > 10^5 cps/mL;
     (HBV DNA assays are poorly standardized and should be interpreted cautiously. The diagnostic threshold of serum HBV DNA of 10^5 cps/mL or greater is somewhat arbitrary, but helps to identify patients with significant infection that is usually associated with liver inflammation.)
  3) persistent or intermittent elevations in ALT levels; and
  4) liver biopsy (when performed) showing necroinflammation score of Knodell ≥ 4.

  Chronic hepatitis B can be characterized as HBeAg-positive or HBeAg-negative. Persons with HBeAg-positive hepatitis have an increased risk of progressive liver disease. Persons with HBeAg-negative chronic hepatitis B have elevated HBV DNA levels and necroinflammation on liver biopsy, despite being HBeAg-negative. HBeAg-negative chronic hepatitis has a fluctuating, less predictable course, compared to HBeAg-positive hepatitis, and occurs more commonly in persons from Asia and Mediterranean countries.

- **Chronic asymptomatic HBV infection:** Certain persons with chronic HBV infection are able to clear HBeAg, with an associated decrease in detectable serum HBV DNA, while remaining HBsAg-positive. These persons are at low risk of developing cirrhosis and have the following diagnostic criteria:

1) HBsAg-positive for > 6 months;
2) HBeAg-negative/anti-HBe-positive;
3) serum HBV DNA < 10^5 cps/mL;
4) persistently normal ALT levels; and
5) liver biopsy (when performed) confirms absence of significant necroinflammation and Knodell score < 4.

- **Resolved hepatitis B (anti-HBs-positive):** A certain proportion of persons with chronic HBV infection spontaneously clear their infection (approximately 1% yearly). Serum HBV DNA levels decrease to undetectable levels (although very low levels may be detectable by PCR), ALT levels normalize, and serum HBsAg disappears.

Chronic hepatitis B flares: Clinically apparent flares of hepatitis B can occur in persons with chronic HBV infection during the following:

1) spontaneous clearance of HBeAg with development of anti-HBe antibodies;
2) superinfection with HBV-HDV (hepatitis delta virus);
3) immunosuppression;
4) initiation of antiviral therapy for chronic hepatitis B; and
5) discontinuation of certain antiviral therapies for chronic hepatitis B or HIV infection.

Chronic hepatitis B complications: Individuals with chronic HBV infection are at increased risk of developing decompensated cirrhosis and hepatocellular carcinoma (HCC). Rates of progression to cirrhosis or HCC are affected by a variety of factors, including: HBeAg positivity, history of alcoholism, co-infections with HIV, HCV, or HDV, and family history of HCC. Non-hepatic complications of HBV infection include membranous glomerulonephritis and polyarteritis nodosa.

Evaluation and Treatment

Baseline evaluation: A baseline clinician evaluation is indicated for inmates who have chronic HBV infection (HBsAg-positive) and should include:

- Targeted history (assess age at initial infection, alcohol and substance abuse history, family history of hepatocellular carcinoma and chronic HBV infection, risks for gastrointestinal bleeding, and symptoms of decompensated cirrhosis);

- Targeted physical examination (assess for evidence of decompensated cirrhosis, such as jaundice, ascites, encephalopathy, asterixis, and peripheral edema);

- Serum ALT, AST, bilirubin, alkaline phosphatase, albumin, prothrombin time, and further diagnostic evaluations as clinically warranted for other potential causes of liver disease, such as hemochromatosis, Wilson's disease, and autoimmune hepatitis;

- CBC with differential and platelet count;

- Renal function assessment (i.e., serum creatinine / BUN);
- HBeAg, anti-HBe;
- HBV DNA nucleic acid test (HBV DNA assays are poorly standardized; therefore data should be interpreted cautiously);
- Screening for other bloodborne pathogens, e.g., anti-HIV, anti-HCV, and anti-HDV; and
- Hepatitis A vaccination with priority should be given to inmates with underlying liver disease. (Prescreening for immunity to HAV, by detecting IgG (or total) anti-HAV, should be considered prior to vaccination for Native American populations and foreign-born inmates from Latin America, Africa, Southeast Asia, and China where HAV infection is endemic, and for inmates 50 years of age or older).

Hepatocellular carcinoma (HCC) screening: HCC occurs in persons with chronic HBV infection with or without cirrhosis. **For patients with chronic HBV infection, both the benefits of HCC screening and the optimal screening strategy are uncertain.** Based upon available data, the screening strategy outlined below should be considered on a case-by-case basis. The following groups of inmates with chronic HBV infection, who are at higher risk for HCC, should be screened periodically by obtaining a liver ultrasound or computed tomography (CT) scan (e.g., annually) and alpha-fetoprotein (e.g., every 6 months):

- Inmates with cirrhosis
- Inmates with a family history of HCC

For male inmates who are 45 years of age or older and inmates from countries where chronic HBV infection is endemic, obtain a baseline alpha-fetoprotein screen. Consider periodic repeat alpha-fetoprotein screening (e.g., annually) for these inmates.

Periodic evaluations: Clinician evaluations for inmates with chronic HBV infection should be scheduled on a case-by-case basis in consideration of the following:

- **Chronic HBV infection (HBeAg-positive or HBeAg-negative/HBV DNA-positive) with elevated ALT levels > 2 times the upper limit of normal**: Refer for liver biopsy and possible antiviral therapy, and monitor as clinically necessary.
- **Chronic HBV infection (HBeAg-positive) with normal or mildly elevated ALT levels:** Monitor ALT levels every 3-6 months/HBeAg annually to determine if patient is developing worsening liver disease or clearing HBeAg. (ALT levels may transiently increase with clearance of HBeAg and the development of anti-HBe.)

- **Asymptomatic chronic HBV infection (HBeAg-negative/HBsAg-positive/HBV DNA < 10^5 cps/ml):** Monitor ALT levels every 6-12 months/HBsAg annually for spontaneous clearance, i.e., resolution of infection (HBsAg-negative).

- **Resolved chronic HBV infection** (anti-HBs positive)**:** Discontinue from chronic care clinic.

Treatment considerations: A thoughtful, case-by-case approach to initiating antiviral therapy for chronic hepatitis B is warranted, in consultation with a physician expert, for the following reasons:

- The risks and benefits of long-term treatment are unknown;

- The potential for drug resistance is of concern with some treatments;

- Discontinuing therapy in some persons responding to treatment may result in relapse;

- A subset of infected persons spontaneously clear HBV infection without therapy in placebo-controlled trials; and

- Future treatment options may be more effective, better tolerated, and more easily administered.

The decision to recommend antiviral treatment should be based on the severity of liver disease, the likelihood of response, existing co-morbid conditions, the potential for adverse reactions, and other relevant patient-specific factors.

Treatment indications: Indications for treating chronic hepatitis B with antiviral therapy should include all of the following:

- Chronic HBV infection (HBsAg-positive) documented for at least 6-12 months duration;

- Evidence of active viral replication, i.e., HBV DNA > 10^5 cps/ml (HBeAg-positive/HBV DNA-positive or HBeAg-negative/HBV DNA-positive);

- Chronic liver inflammation suggested by elevated ALT levels (> 2 times the upper limit of normal); and

- Evidence of necroinflammation on liver biopsy with a Knodell score ≥ 4.

Antiviral options: Approved antiviral therapies for chronic hepatitis B include interferon alfa-2b, pegylated interferon alfa-2a, adefovir dipivoxil, entecavir, and lamivudine. Dosaging, potential side effects, and monitoring parameters are outlined in *Appendix 4 (Antiviral Medications for Chronic Hepatitis B).*

- **Interferon preparations: Pegylated interferon alfa-2a or interferon alfa-2b** can be administered for a shorter duration (≤ 12 months) and are less likely to promote resistance compared to other therapies. Disadvantages of interferon therapy include its subcutaneous administration, the risk of hepatic decompensation when treating persons with cirrhosis, and the potential for serious side effects including neuropsychiatric symptoms, bone marrow suppression, and thyroid disease.

  Predictors of a favorable response to interferon therapy include the following factors:

  - Short duration of disease;
  - High pretreatment ALT levels;
  - Low serum HBV DNA levels;
  - Liver necroinflammation on biopsy; and
  - Absence of renal failure, HIV infection, or other serious co-morbidity.

- **Adefovir dipivoxil and entecavir** are oral antiviral agents that are easy to administer, have limited toxicities, are less likely to promote viral resistance compared to lamivudine, and have some efficacy against lamivudine-resistant HBV mutants. **The major disadvantage of these agents is that the optimal treatment duration is very difficult to determine. Cessation of therapy can result in viral relapse or severe hepatitis in certain patients.** Long-term therapy is likely required for many patients. Duration of therapy with these medications should be discussed with a physician expert.

  Adefovir dipivoxil is generally well tolerated at the recommended 10 mg dose without the associated renal toxicity observed at higher doses. Persons with underlying renal insufficiency and those on long-term therapy, however, are potentially at increased risk for nephrotoxicity. Entecavir, although renally excreted has not been associated with nephrotoxicity. Life threatening lactic acidosis and severe hepatomegaly are potential adverse reactions of both adefovir dipivoxil and entecavir. Adefovir dipivoxil has weak activity against HIV, whereas entecavir does not.

- ***Lamivudine*** *is an oral antiviral agent that is an increasingly less attractive treatment option* for hepatitis B due to its lack of long term efficacy and its strong association with drug-resistant mutants that may limit treatment gains or actually worsen liver disease. Lamivudine should not be combined with interferon or other antiviral agents for hepatitis B, since there is no proven benefit. Inmates previously started on lamivudine should not be discontinued without consulting a physician expert due to the risk of precipitating liver failure.

Monitoring treated inmates: Inmates receiving antiviral therapy for chronic hepatitis B should receive clinician evaluations consistent with the following:

- Clinician evaluations weekly for one month, then monthly thereafter, to assess drug side effects and potential disease complications;

- Psychiatry or psychology evaluations as clinically indicated during interferon treatments;
- ALT at weeks 1, 2, and 4, and at 4-8 week intervals thereafter;
- Periodic bilirubin, prothrombin time and other liver function studies as clinically warranted;
- Creatinine and BUN periodically (more frequently while on adefovir or tenofovir DF);
- CBC with differential and platelet count at weeks 1, 2, and 4 and at 4-8 week intervals thereafter; and
- Thyroid function studies every 3 months during interferon therapy.

Transient increases in aminotransferase levels are common during therapy and correlate with immune system clearance of HBV and the disappearance of HBeAg. Mild to moderate increases in liver enzymes should not be an indication for reducing or discontinuing interferon therapy, unless associated with deteriorating liver synthetic function or jaundice.

Evaluating treatment response: The effectiveness of antiviral therapy for chronic hepatitis B is determined by monitoring the following parameters:

1) absence of HBeAg (if HBeAg-positive)
2) absence of HBV DNA
3) normalization of ALT

The clearance of HBeAg in persons with chronic HBe-positive hepatitis is associated with improved clinical outcomes. HBeAg may not disappear, however, for months or longer after the completion of effective antiviral therapy. HBsAg may remain positive and HBV DNA may remain detectable for years after completion of treatment. The long-term clinical consequences of persistent viremia are uncertain. Monitoring treatment response is even more difficult in persons with HBe-negative hepatitis. Clearance of viremia and normalization of ALT with treatment are helpful signs, but relapse is common in these patients despite an initial favorable response.

Decompensated cirrhosis: Patients with decompensated cirrhosis have evidence of severe liver disease such as markedly impaired synthetic function and signs of portal hypertension. Interferon preparations are contraindicated in these patients due to an increased risk of inducing hepatic failure. Chronic monotherapy with lamivudine, or adefovir, or entecavir can be considered for these patients, since these agents may reduce the incidence of hepatic failure and hepatocellular carcinoma. Once instituted, these agents should ordinarily not be discontinued, due to the risk of precipitating hepatic failure.

Complicating medical conditions: Inmates with chronic hepatitis B and the following complicating medical conditions warrant special consideration.

- **HBV and HCV co-infection:** Interferon preparations are effective against hepatitis B and C, but the efficacy, optimal regimen, and indications for treating hepatitis with underlying HBV and HCV infections are unknown. Antiviral therapy for chronic hepatitis B in inmates co-infected with HCV should only be initiated after consultation with a physician expert, and with great caution, due to the lack of a recommended treatment strategy and the uncertain effects on underlying liver disease.

- **HBV and HIV co-infection:** Concurrent infection with HIV increases the risk of cirrhosis in persons with HBV infection. Conversely, HBV infection does not hasten the progression of HIV infection to AIDS. Antiviral therapy for chronic hepatitis B in inmates co-infected with HIV can be considered on a case-by-case basis in consultation with a physician expert, while considering the following:

  - No long-term, evidence-based data are available to guide treatment decisions for these patients.
  - Interferon alfa therapy for chronic hepatitis B is less effective in persons with HIV/HBV co-infection, compared to persons without HIV infection. The advantages of interferon therapy, over other treatment options, include the limited duration of therapy, and the lack of antiretroviral activity.
  - Tenofovir disoproxil fumarate (DF), emtricitabine, tenofovir DF combined with emtricitabine (Truvada®), and lamivudine are all active against both HIV and HBV. Patients with HBV/HIV infections who are not candidates for antiretroviral therapy, but who are candidates for treatment of chronic hepatitis B, should ordinarily **not** be treated for hepatitis with these agents, since it will promote HIV resistance to these drugs that may be needed for future HAART.
  - Adefovir dipivoxil has weak activity against HIV at the doses used to treat chronic hepatitis B. There is a theoretical risk of inducing cross resistance to tenofovir; therefore, adefovir dipivoxil is not an optimal treatment choice for hepatitis B in persons with HIV co-infection.
  - Entecavir does not have activity against HIV infection. For this reason, it may be a treatment option which does not compromise future HAART. However, data on use of entecavir for treating HIV/HBV co-infected patients are limited.
  - Persons with HIV/HBV co-infections who are candidates for HAART should ordinarily be treated with a HAART regimen that includes an agent that is also active against HBV, i.e., tenofovir DF. The degree of underlying liver disease should also be considered when weighing the need to concurrently treat hepatitis B and HIV infection.

- **Renal disease:** Renal insufficiency secondary to glomerulonephritis from HBV infection may respond to interferon therapy; however, treatment should be considered in consultation with a physician expert making dosage adjustments made as necessary. Neither adefovir nor lamivudine should be used to treat chronic hepatitis B in patients with renal insufficiency.

Hepatitis B Prevention

Vaccine program and indications: Each institution should establish a hepatitis B vaccine program for inmates, since persons at risk of acquiring HBV infection are over represented among inmate populations. The BOP targets the following inmates for hepatitis B vaccination, based on risk of infection and co-morbid conditions:

- Inmates on chronic hemodialysis or inmates with evolving end-stage renal disease for whom future hemodialysis is anticipated;
- Pregnant women (previously unvaccinated HBsAg-negative mothers);
- As a component of post-exposure prophylaxis for unprotected inmates following percutaneous or permucosal exposures to blood, including victims of sexual assault;
- Inmate workers at risk for bloodborne pathogen exposure in accordance with the institution's exposure control plan and applicable federal regulations;
- Contacts of inmates diagnosed with acute hepatitis B within the context of a contact investigation;
- Recipients of clotting factor concentrates;
- Inmates with HIV infection with risk factors for acquiring HBV infection;
- Inmates with chronic HCV infection;
- Inmates with cirrhosis or liver disease;
- Inmates with history of injection drug use;
- Male inmates who have sex with men; and
- Inmates with history of syphilis, gonorrhea or chlamydia in the last 2 years.

Vaccine administration: Hepatitis B vaccine is available as ENGERIX-B® or RECOMBIVAX HB®. These products are interchangeable, i.e., a vaccination series begun with one product may be completed with the other. Hepatitis B vaccine is also available in a combined formulation with hepatitis A vaccine (TWINRIX®). Viral hepatitis vaccines are listed in *Appendix 5 (Viral Hepatitis Vaccine Doses and Schedules)*. **Hepatitis B vaccination should be administered in accordance with the following guidelines:**

- **Prevaccination serologic screening for immunity to HBV infection is not routinely recommended**, but should be considered on a case-by-case basis. Serologic screening is only cost-effective if the probability of prior immunity is high (> 25%), such as in inmates

who report prior hepatitis B vaccination (screen for anti-HBs), as well as in inmates from countries and communities where HBV infection is endemic, i.e., Asia, the South Pacific, sub-Saharan Africa, and certain populations in the Arctic, South America, and the Middle East **(screen for anti-HBc)**.

- **A previous anaphylactic reaction to baker's yeast or to hepatitis B vaccine are contraindications** to vaccination or booster vaccination.

- **Pregnancy should not be considered a contraindication** to vaccination for women at risk of acquiring HBV infection, since HBV itself poses a significant risk to the fetus or newborn. No apparent risk exists for adverse effects to developing fetuses when hepatitis B vaccine is administered to pregnant women. Pregnant inmates who are candidates for vaccination should be counseled regarding the risks and benefits of vaccination during pregnancy.

- **All inmate candidates for vaccination should receive counseling** by a physician or otherwise qualified health care provider on the administration and potential adverse reactions to hepatitis B vaccination. Counseling, consent, and declination should be documented as per BOP policy.

- **The three-dose vaccination series is ideally administered at 0, 1, and 4-6 months.** However, there is significant flexibility with the administration of the complete series with the following guidelines: There must be at least a 1-month interval between doses #1 and #2; and at least a 2-month interval between doses #2 and #3; and at least a 4-month interval between doses #1 and #3. If a dose is delayed, the next dose should be administered without restarting the entire series.

- **The vaccine is administered intramuscularly in the deltoid muscle.**

- **Postvaccination testing (anti-HBs) to determine antibody responder status is not routinely indicated** for newly vaccinated inmates, unless future exposures to HBV are anticipated, e.g, inmates receiving hemodialysis and inmate workers with anticipated exposures to blood.

Inmate workers: Inmate workers with potential exposure to infectious blood or body fluids (as determined by the institution's bloodborne pathogen exposure control plan) should be offered hepatitis B vaccination in accordance with BOP policy. Newly vaccinated inmate workers should have anti-HBs levels measured 1-2 months after the third dose of vaccine. Inmates with low levels of anti-HBs (< 10 mIU/mL) should receive a second 3-dose hepatitis B vaccine series with repeat antibody testing 1-2 months after the third dose of vaccine. Inmate workers who still have low levels of anti-HBs after receiving the second hepatitis B vaccine series should be considered nonresponders susceptible to HBV infection. They should be counseled regarding appropriate preventive measures and the need for post-exposure HBIG prophylaxis despite vaccination.

Hemodialysis patients: Inmates on chronic hemodialysis are at risk for ongoing exposures to HBV and require hepatitis B vaccination, along with close monitoring of their immune status in accordance with the following:

- **Inmates on hemodialysis require higher doses of hepatitis B vaccine with different administration schedules,** compared to standard recommendations for hepatitis B vaccine *(Appendix 5)*.

- **Inmates on hemodialysis who are newly vaccinated for hepatitis B should have anti-HBs measured 1-2 months after the last dose of vaccine.** Inmates with low levels of anti-HBs (< 10 mIU/mL) should receive a second hepatitis B vaccine series with repeat antibody testing 2 months after the last dose of vaccine. If anti-HBs levels remain low, the inmate should be considered a nonresponder susceptible to HBV infection, and should be counseled regarding appropriate preventive measures. Nonresponders and susceptible inmates who refuse vaccination should be monitored for newly acquired HBV infection while on dialysis by measuring HBsAg monthly.

- **Those with adequate anti-HBs (≥ 10 mIU/mL) following vaccination, but who are anti-HBc negative (no natural immunity), should have anti-HBs monitored annually.** A booster dose of vaccine should be administered if the anti-HBs falls below 10 mIU/mL.

- **Inmates on hemodialysis with a history of HBV infection** (anti-HBc-positive and anti-HBs-positive or HBsAg-positive) **do not require anti-HBs monitoring or consideration for vaccination.**

- **Inmates receiving hemodialysis who test positive for anti-HBc alone could have a false positive test, low-grade chronic infection, remote infection, or resolving acute infection.** These hemodialysis patients should be evaluated in accordance with CDC guidelines (per the algorithm in *MMWR* 2001;50(RR-5) to assess their status so that the appropriate monitoring, immunization, and infection control measures can be determined.

Infection Control

Patient education: During orientation to the institution, and as appropriate during clinical evaluations, all inmates should be counseled about the importance of preventing blood exposures during activities of daily living, i.e., sharing toothbrushes and razors and through unsafe behaviors such as injection drug use, tattooing, and sexual contact with other inmates.

Reporting: Each institution should have a surveillance system for notifiable infectious diseases in accordance with BOP policy. All cases of acute hepatitis B should be reported to state health authorities as required by all states and the Commonwealth of Puerto Rico. Inmates with chronic HBV infection should be reported to the local and state authorities, as required. All acute cases of hepatitis B and any HBsAg seroconversions among hemodialysis patients should be reported to the Central Office HSD.

Containment: Inmates with acute hepatitis B and chronic HBV infection (HBsAg-positive) do not require isolation, but should be counseled on the specific measures necessary for preventing further transmission of HBV to others during incarceration and upon release, and should be managed while incarcerated using standard infection control precautions. Non-disposable, patient-care items must be appropriately cleaned, disinfected, or sterilized based on the use; and measures must be taken to prevent cross-contamination during patient care, e.g., dialysis, vascular access, cauterizing, and dental procedures, in accordance with CDC guidelines.

Hemodialysis: Infection control measures should be implemented to reduce the transmission of HBV during hemodialysis in accordance with CDC guidelines for preventing transmission of bloodborne pathogen infections among hemodialysis patients (*MMWR* 2001;50(RR-5)).

- **Screening and prevention:** All inmates receiving chronic hemodialysis should be screened for prior HBV infection before admission to the hemodialysis unit by measuring the following serologic markers: HBsAg, total anti-HBc, and anti-HBs. Those inmates found to be susceptible to HBV infection should receive hepatitis B vaccine in accordance with CDC guidelines. For both patient care and surveillance purposes, all hemodialysis inmates who remain susceptible to HBV infection, i.e, nonresponders, should be screened monthly for HBsAg seroconversion.

- **Infection control measures:** Institutions that provide dialysis should establish written policies and practices and a mechanism for review, update, and training of staff to ensure that infection control measures to reduce the transmission of HBV during hemodialysis are implemented including the following:

  - Specifically assigned stations or isolation room, chairs, medications, supplies, and designated staff (do not care for HBV-susceptible inmates at the same time) should be used to separate HBsAg-positive inmates from HBsAg-negative inmates.
  - HBsAg-positive inmates should be dialyzed on specifically dedicated machines. Dialyzers from HBsAg-positive inmates should not be reused.
  - If it is necessary to reuse a machine used by a HBsAg-positive inmate for a HBsAg-negative inmate, internal pathways of the machine can be disinfected using conventional protocols and external surfaces cleaned using soap and water or a detergent germicide.
  - All machines and station areas that are used on HBsAg-positive inmates must be terminally cleaned after each use (refer to manufacturers' instructions and CDC recommendations).

Blood glucose monitoring: Patient-to-patient transmission of HBV can readily occur when performing routine diabetes-care procedures, if appropriate infection control practices are not used. CDC recommendations should be consistently implemented, including standard precautions, strict hand hygiene practices, use of insulin preparation and glucometer maintenance procedures that prevent cross contamination, ensuring adequate training of staff, and promptly and thoroughly investigating any new HBV infection among diabetic inmates.

Whenever feasible, individual inmates should be assigned their own glucometer for use. If reused with another inmate, the glucometer must be cleansed and disinfected between each use.

Contact investigations: An internal contact investigation is required for inmates diagnosed with acute hepatitis B (IgM anti-HBc-positive), who were incarcerated during the 6 weeks - 6 months prior to disease onset, in order to identify other inmates acutely infected with HBV and better target post-exposure management of asymptomatic contacts. Close contacts should be tested for HBsAg to help identify the source case. Aggressive "ring vaccination" of close contacts is warranted. The contact investigation should be coordinated with local and state health departments. Contact investigation tools are attached in *Appendix 6a (Contact Investigation - Acute Hepatitis B)* and *Appendix 6b (Line Listing - Acute Hepatitis B)*.

Asymptomatic inmates with positive IgM anti-HBc serologies should be first evaluated to assess if the inmate was symptomatic with acute hepatitis B or infected with HBV before or after incarceration. (IgM anti-HBc can remain positive several years after acute infection.) A contact investigation should be pursued if HBV infection was acquired while the inmate was incarcerated. If the infection was acquired prior to incarceration, the local and state health authorities should be notified as required.

Ongoing assessments of transmission: Inmates diagnosed with chronic HBV infection (HBsAg-positive) should be interviewed at the time of diagnosis and periodically thereafter during chronic care and prevention visits to determine if they have exposed other inmates to infected blood through sharing toothbrushes and razors, through injection drug use, tattooing, or sexual contact with other inmates. Identified contacts should be considered for post-exposure prophylaxis.

Post-exposure management: Inmates with percutaneous (e.g., injection drug use, tattooing, injury with needle or needle-like device contaminated with blood of unknown origin) or mucosal (e.g., sexual contact, human bites) exposures to blood warrant emergency evaluation for post-exposure prophylaxis. In evaluating human bites, both the person bitten and the biter should be considered exposed to blood.

- **Emergent care:** Wounds and skin sites that have been in contact with blood or bloody body fluids should be washed with soap and water. Exposed mucous membranes should be flushed with water. Squeezing the wound and treating with topical antiseptics are not recommended.

- **Counseling:** Inmates with percutaneous or mucosal exposures to blood should be assessed by a health care provider and counseled regarding their risk of HBV infection, the natural history of HBV infection, and the recommendations for post-exposure prophylaxis.

- **Post-exposure interventions:** Prompt post-exposure prophylaxis should be provided to inmates potentially exposed to HBV in accordance with the following:

- Unvaccinated inmates should begin the vaccine series immediately and subsequent doses should be administered in accordance with standard practices. Exposed inmates who have already begun, but not completed, the vaccine series should receive subsequent vaccine doses as previously scheduled.
- The source of the exposure should be tested for HBsAg, even if that person was previously vaccinated.
- If the source of the exposure is HBsAg-positive, hepatitis B immunoglobulin (HBIG) 0.06 mL/kg body weight should also be administered to unvaccinated exposed inmates, as soon as possible, but <7 days after the exposure. (When administered simultaneously, hepatitis B vaccine and HBIG should be given intramuscularly at separate sites, with the vaccine administered in the deltoid muscle.)
- Inmates who have been fully vaccinated prior to an exposure to HBV ordinarily do not require post-exposure prophylaxis.
- Inmates who have been fully vaccinated prior to an exposure to HBV may warrant a vaccine booster and/or HBIG, as outlined in *Appendix 7 (Management of HBV Exposures)* if their anti-HBs responder status has previously been determined (e.g., hemodialysis patients, certain inmate workers), or their responder status is newly assessed because of unique circumstances surrounding the exposure.
- In the context of a contact investigation of acute hepatitis B cases, both hepatitis B vaccination and HBIG are indicated for inmates who have had percutaneous or mucosal exposures to blood; whereas hepatitis B vaccination alone is indicated for other close inmate contacts who have not had direct percutaneous or mucosal exposures.

4. Hepatitis C Virus (HCV)

Transmission

Hepatitis C virus (HCV) is a single-stranded, enveloped, RNA virus with 6 genotypes and more than 50 subtypes. Genotype 1 is predominant in the United States. HCV is transmitted primarily by direct percutaneous exposures to infectious blood, such as through injection drug use or the transfusion of contaminated blood products (prior to July 1992). HCV is inefficiently transmitted through sexual contact; however, persons with a history of sexually transmitted diseases and/or multiple sexual partners have an increased risk of acquiring HCV infection. HCV is transmitted from mother to child in approximately 5-6% of pregnant women who have chronic HCV infection at the time of delivery. Breast feeding does not transmit HCV from an infected mother to her child. Tattooing with shared, contaminated needles or needle-like devices in jails and prisons is a potential mode of HCV transmission that may affect inmate populations. Intranasal cocaine use may be a risk factor for acquiring HCV infection, but its exact role in transmission remains ill-defined. HCV is not spread by kissing, sneezing, hugging, coughing, food or water, sharing eating utensils or drinking glasses, or other casual contact.

Most inmates diagnosed with HCV infection have behavioral risk factors for acquiring HCV and were infected prior to incarceration. Low levels of HCV transmission between inmates have been documented through seroincidence studies and contact investigations; however, large HCV outbreaks have not been reported in the correctional setting.

Acute Hepatitis C Infection

Diagnosis

Acute HCV infection is diagnosed when there is circumstantial evidence for new infection, such as a recent exposure to a known HCV-infected inmate or clinical features of acute hepatitis (jaundice, nausea, anorexia, and malaise) with the exclusion of other causes of hepatitis. Acute hepatitis C rarely causes fulminant hepatic failure.

The mean incubation period from transmission of HCV infection to the onset of symptoms is 6-7 weeks (range: 2-26 weeks); however, only 20-30% of newly infected persons are symptomatic. Serum ALT levels increase 4-12 weeks after acute HCV infection. Antibodies to HCV (anti-HCV) may or may not be present when symptoms develop or with elevations in ALT levels; however, after 3 months of HCV infection, anti-HCV is detectable by immunoassay in 90% of patients.

The diagnosis of acute hepatitis C is confirmed by:

1) **marked elevations in ALT** (> 7 times the upper limit of normal) with or without symptoms of acute hepatitis;
2) **negative tests for acute hepatitis A** (IgM anti-HAV) **and acute hepatitis B** (IgM anti-HBc); and
3) **a positive anti-HCV screening immunoassay** (enzyme immunoassay, EIA or chemiluminescence immunoassay, CIA) that is confirmed with either:
   - an immunoassay with a signal-to-cutoff ratio predictive of a true positive for that assay; or
   - a supplemental test, e.g., recombinant immunoblot assay (RIBA®).
     (HCV RNA may be detected by a qualitative viral load test in the blood 1-3 weeks after exposure, but viremia may be transient, i.e., a negative qualitative HCV RNA does not preclude acute HCV infection.)

Testing recommendations following a known exposure:

1) **nucleic acid test for HCV RNA** immediately after exposure, at week 4 and at week 12;
2) **anti-HCV by EIA or CIA** immediately after exposure and at week 12; and
3) **serum ALT and AST** immediately after exposure, at week 4 and at week 12.

Treatment

Inmates diagnosed with acute hepatitis C should be considered for antiviral therapy in consultation with a physician with expertise in managing hepatitis. Reported data suggest that antiviral therapy is beneficial in treating persons with acute HCV infection; however, the timing and the optimal treatment regimen in this setting are uncertain. Therefore, treatment decisions should be made on a case-by-case basis. In one study, 52% of symptomatic individuals with acute hepatitis C spontaneously cleared the virus within 12 weeks. Of those who did not clear the virus, treatment initiated within 3-6 months of infection resulted in a sustained virological response in 81%. Thus, the American Association for the Study of Liver Disease (AASLD) guidelines state: "In the absence of controlled study data, no definitive recommendations can be made about the timing of treatment initiation; however, it seems reasonable to delay treatment for 2-4 months after acute onset to allow for spontaneous resolution." Subsequent treatment, if indicated, should consist of pegylated interferon, with or without ribavirin. Optimal treatment duration is unknown; if tolerated, treatment should be given for at least 12 weeks, and then an HCV RNA test obtained to determine treatment response.

Chronic Hepatitis C Infection

Screening

Newly incarcerated inmates should be provided educational information on the transmission, natural history, and medical management of HCV infection by appropriately trained personnel in accordance with BOP policy. The BOP peer-oriented video on infectious diseases, "Staying Alive", and the information in *Appendix 2 (Inmate Fact Sheet: Hepatitis B and C Viral Infection)* and other appropriate patient educational tools should be used to facilitate counseling efforts.

Screening method: The preferred screening test for HCV infection is an immunoassay (e.g., EIA or CIA) that measures antibodies to HCV antigens.

Clinical indications: Inmates should be screened for hepatitis C regardless of sentencing status if any of the following clinical indications exist:

- Inmates on chronic hemodialysis (screen ALT levels monthly and anti-HCV by immunoassay semiannually);
- Inmates with elevated ALT levels of unknown etiology;
- As clinically indicated, e.g., inmates with signs or symptoms of acute or chronic hepatitis or percutaneous blood exposure while incarcerated; and

- Evidence of extrahepatic manifestations of HCV infection such as mixed cryoglobulinemia, membranoproliferative glomerulonephritis, or porphyria cutanea tarda.

Non-sentenced inmates: Screening by immunoassay for HCV infection in asymptomatic, highly mobile, non-sentenced inmates should ordinarily not be pursued unless clinically indicated. Asymptomatic non-sentenced inmates in BOP detention facilities with histories of injection drug use or other high risk behaviors for HCV infection, should be counseled regarding their risk for HCV infection and behaviors that will reduce transmission of HCV infection to others during incarceration and upon release. Referrals to community HCV testing sites should be made when appropriate. Long-term inmates in BOP detention facilities should be screened for HCV infection in accordance with guidelines for sentenced inmates.

Sentenced inmates: An anti-HCV screening immunoassay should be considered for the following sentenced inmates during the prevention baseline visit:

- Inmates who have ever injected illegal drugs or shared equipment;
- Inmates who have received tattoos or body piercings while in jail or prison;
- Inmates with HIV infection or chronic HBV infection;
- Inmates who received a blood transfusion/organ transplant before 1992 or received clotting factor transfusion prior to 1987; and
- Inmates with a history of percutaneous exposure to blood.

Sentenced inmates who have risk factors for HCV infection, but initially refuse testing, should be counseled periodically during preventive health visits on the need for testing during routine patient encounters.

Diagnosis and Counseling

Diagnosis: The detection of anti-HCV by immunoassay in a person with risk factors for acquiring HCV infection strongly predicts prior infection with HCV. A **quantitative** HCV nucleic acid test, however, is required **before initiating antiviral therapy,** regardless of HCV genotype, to both confirm chronic infection and guide therapy. If the quantitative HCV nucleic acid test is negative, the more sensitive qualitative HCV nucleic acid test (lower limit of detection of 50 IU/mL) should be obtained. Other important issues regarding HCV diagnostic assays include:

- The appropriate processing of HCV nucleic acid test samples is essential, since viral RNA is unstable and false negative tests may result from inadequate processing.
- The RIBA® supplemental test is not routinely recommended for diagnosing chronic HCV infection.

Patient counseling: Inmates diagnosed with chronic HCV infection should be counseled by a health care provider about the natural history of the infection, potential treatment options, and specific measures for preventing transmission of HCV infection to others (during incarceration and upon release), including the following information and recommendations:

- Most persons with chronic HCV infection will *remain* healthy, but a small number of persons will develop serious liver disease. Talk to your health care provider about your personal health status and risk of liver disease.

- Current drug treatment options for chronic hepatitis C are moderately effective. Newer medications should be available in the future that will improve treatment options. Medications may or may not be appropriate for you at this time. Talk to your doctor about your specific treatment plan.

- Do not inject drugs, have sex with other inmates, or get a tattoo or body piercing while in prison. Individuals who continue to inject drugs should be counseled to avoid reusing or sharing syringes, needles, water, and cotton or other paraphernalia.

- Do not share personal items that might have your blood on them, such as toothbrushes, dental appliances, nail-grooming equipment or razors.

- Cover cuts and skin sores to keep blood from contacting other persons.

- Before release, talk to a health care provider about specific ways you can reduce the risk of transmitting HCV infection to others after you are released.

- For the remainder of your life, do not drink alcohol at all, or only rarely, and speak to a physician prior to taking any new medications, including over-the-counter medications such as nonsteroidal anti-inflammatory drugs (NSAIDs) and herbal remedies, that may damage your liver.

- Upon release, do not donate blood, body organs, other tissue or semen.

- Upon release, seek medical attention so that you receive appropriate monitoring and treatment of your condition.

Natural History

An estimated 50-85% of persons infected with HCV develop chronic infection, while 15- 50% of newly infected persons are able to clear the virus spontaneously. Chronic HCV infection frequently results in high levels of HCV RNA in the blood, ranging from 10^5-10^7 international units (IU)/mL, despite the presence of HCV antibodies. The majority of persons with chronic HCV infection are asymptomatic.

Chronic HCV infection has an unpredictable course that is frequently characterized by fluctuations in ALT levels that may or may not be associated with significant liver disease. Approximately one-third of persons with chronic HCV infection have no laboratory or biopsy evidence of liver disease.

An estimated 10-15% of persons with chronic HCV infection develop progressive fibrosis of the liver leading to cirrhosis. High levels of alcohol consumption, older age at the time of infection, HIV infection, chronic HBV infection, and male gender increase the risk of disease progression. The degree of viremia ("viral load") and the HCV genotype, however, do not affect the progression of liver disease. The degree of ALT elevation does not strongly correlate with the risk of disease progression, but persons who develop cirrhosis are more likely to have marked elevations in serum ALT levels. Once cirrhosis develops in persons with chronic HCV infection, the risk of hepatocellular carcinoma (HCC) is about 1-4% per year.

Evaluation and Treatment

Baseline evaluation: A baseline clinician evaluation should be conducted for all inmates diagnosed with HCV infection and include at least the following:

- Estimation and documentation of the earliest possible date of infection (whenever feasible);
- Targeted history and physical examination to evaluate for signs and symptoms of liver disease, quantify prior alcohol consumption and determine risk behaviors for acquiring HCV infection;
- Serum ALT, AST, bilirubin, alkaline phosphatase, albumin, prothrombin time, and further diagnostic evaluations as clinically warranted, for other potential causes of liver disease such as hemochromatosis, Wilson's disease, and autoimmune hepatitis;
- CBC with differential and platelet count;
- Renal function assessment (serum creatinine / BUN); and
- Anti-HIV by immunoassay and HBsAg.

Preventive measures: The following preventive interventions are indicated for inmates diagnosed with chronic HCV infection:

- **Hepatitis B vaccination:** Serologic prescreening for immunity to HBV infection should be considered for inmates who self-report previous, but undocumented hepatitis B vaccination by measuring anti-HBs. It is cost-effective to screen inmates from countries where HBV infection is endemic, e.g., Asia, the South Pacific, sub-Saharan Africa, and certain populations in the Arctic, South America, and the Middle East, by measuring total anti-HBc. Vaccination of inmates not in one of the above two categories should be offered

without prescreening for prior infection. Inmates with evidence of liver disease should be priority candidates for vaccination.

- **Hepatitis A vaccination:** Serologic prescreening for immunity to HAV infection by testing for IgG (or total) anti-HAV should be considered for Native American inmates and foreign-born inmates from Latin America, Africa, Southeast Asia, and China where hepatitis A is endemic, and among inmates 50 years of age or older. All other inmates should be offered vaccination without prescreening for prior infection. Inmates with evidence of liver disease should be priority candidates for vaccination. The combination hepatitis A/B vaccine (Twinrix®) is a convenient and cost-effective option for inmates requiring vaccination against both viruses.

- **Pneumococcal vaccine and yearly influenza vaccination** should be offered for inmates who have developed cirrhosis.

- **Hepatocellular carcinoma (HCC) screening:** Inmates with chronic HCV infection are at increased risk for HCC, but **the optimal screening strategy is uncertain**. Periodic screening for HCC, with a liver ultrasound or abdominal CT-scan (e.g., annually) and serum alpha-fetoprotein (e.g., every 6 months), should be considered for inmates with HCV infection and cirrhosis.

- **Screening for esophageal varices** should be considered in any inmate with known cirrhosis, and in those with suspected cirrhosis who may not be candidates for liver biopsy (e.g., serum markers for impaired hepatic synthetic function, severe thrombocytopenia).

Detention center/short-term inmates: Inmate candidates for hepatitis C treatment entering BOP short-term detention facilities, including pre-trial and nonsentenced federal detainees, should ordinarily **not** be started on antiviral therapy. The potential for interrupted antiviral therapy for hepatitis C places the inmates at risk for a number of undesirable outcomes, including treatment failure if the course of treatment is not completed, and adverse effects from medications if the inmate does not receive the required laboratory and clinical monitoring upon release or transfer.

Inmates entering BOP custody who are already on treatment for hepatitis C, should be maintained on antiviral therapy, unless treatment must be discontinued for medical reasons. Consult with a Central Office physician if there are questions regarding continuation of therapy.

Treatment considerations: Treating physicians should weigh the following factors in assessing the appropriateness of treatment and the best timing for initiating treatment as they counsel inmates with chronic HCV infection:

- Only 10-15% of persons with HCV infection develop significant long term complications of liver disease, usually 20-30 years after initial infection.

- No laboratory parameters definitively predict which persons infected with HCV will develop cirrhosis or will respond to medical therapy.

- The presence of moderate to severe fibrosis (Metavir ≥ stage 2 or Ishak ≥ stage 3) on liver biopsy is currently the best marker for determining who should be offered antiviral therapy for hepatitis C.

- The combination of a pegylated interferon plus ribavirin is significantly more effective in clearing viremia and establishing sustained viral response rates (SVR) than prior treatment regimens.

- Although current antiviral therapy is usually well tolerated, serious drug side effects may occur.

- Future treatments for hepatitis C may be more effective and more easily tolerated.

An evidenced-based strategy for evaluating inmates for hepatitis C treatment is outlined in *Appendix 8 (Step-Wise Approach for Evaluating and Treating Chronic Hepatitis C).*

Treatment contraindications and considerations: Inmates with chronic HCV infection who are potential candidates for antiviral therapy should first be assessed for absolute or relative treatment contraindications as listed in *Appendix 9 (Contraindications to Interferon or Ribavirin Therapy)*. Inmates with contraindications to antiviral therapy should not be treated with interferon and ribavirin as long as the contraindication exists.

The following co-morbidities, although not absolute contraindications, should be carefully evaluated prior to initiating antiviral therapy:

- **Mental illness:** Inmates with a history of psychiatric illness or with signs or symptoms of mental illness should be referred to a psychologist or psychiatrist for assessment. Inmates with serious mental illness should be treated and stabilized prior to pursuing a further work-up for treatment.

- **Alcohol:** HCV-infected inmates being considered for treatment who have significant alcohol abuse histories should receive specific counseling messages. Heavy and prolonged alcohol use is an independent risk factor for the development of cirrhosis, and alcohol accelerates the progression of HCV-related fibrosis. Therefore HCV treatment without abstinence from alcohol is unlikely to be of benefit. The treatment response to peginterferon plus ribavirin is significantly reduced in individuals who drink more than 30 grams of alcohol per day, and perhaps with lower levels of consumption, as well.

  An inmate's unwillingness to abstain from alcohol intake while incarcerated is a potential indicator of alcoholism and should be evaluated. Effective treatment for alcoholism should be offered to as many HCV-infected inmates as possible prior to release, whether or not they have been administered HCV treatment or responded to such treatment.

- **Substance abuse:** Inmates with significant substance abuse other than alcohol may have a number of issues which can indirectly affect whether HCV treatment will be successful. Injection drug users may also be at risk for HIV, HBV, endocarditis, and possible re-infection with HCV. Amphetamine and cocaine abuse may result in cardiovascular complications which carry morbidities in and of themselves, in addition to the additive risks of interferon and ribavirin. Ongoing substance use in the controlled environment of a prison or jail is, at best, an indicator that the inmate is not taking adequate responsibility for his or her overall health. Treatment decisions must be individualized where these issues are present.

Confirmation of infection: Inmate candidates for liver biopsy and/or antiviral therapy should have chronic HCV infection confirmed (if not done previously) through the detection of HCV RNA by a **quantitative** nucleic acid test. A single negative test should be repeated with the more sensitive **qualitative** nucleic acid test to confirm infection.

Genotype determination: The HCV genotype markedly affects treatment response. Persons with genotypes 2 or 3 have a 76-82% response rate to pegylated interferon/ribavirin therapy, compared to persons with genotype 1 who have a 40-45% response rate. The HCV genotype must be determined prior to pursuing treatment, since the genotype will affect patient counseling, the evaluation strategy, the decision to treat for a subset of patients, and the recommended drug regimen. Once the HCV genotype has been determined in a specific patient, serial genotype testing is not indicated unless re-infection is suspected, since HCV genotypes do not change during the course of an infection.

Identifying candidates for liver biopsy: Liver biopsy is the best means of staging liver disease in patients with chronic hepatitis C and may identify other etiologies of chronic liver disease, such as autoimmune hepatitis, alcoholic liver disease, Wilson's disease, and hemochromatosis. Determining the degree of liver disease is particularly important for those inmates who may wish to defer treatment if they have normal liver histology or minimal fibrosis, as well as in cases where relative contraindications to treatment exist, i.e., psychiatric and substance abuse disorders not in full remission, and medical conditions such as diabetes or cardiovascular disease which are not fully controlled. The following guidance should be considered when determining the need for liver biopsy:

- **ALT levels**: The decision to obtain a liver biopsy should not be strongly based on ALT levels; however, ALT levels are a relevant factor that warrant monitoring and review. The greater the ALT level, the more likely it is that a person has significant liver disease; therefore, inmates with markedly elevated ALT levels should be prioritized for liver biopsy. However, even persons with normal ALT levels may have liver disease and should be evaluated for liver biopsy since a small, but significant percentage (14-24%) of persons with normal ALT levels have more than portal fibrosis (Metavir ≥ stage 2).

  Inmates with persistently normal ALT levels (at least 6 normal values evenly distributed over a 24-month period), and who have no other physical or laboratory evidence of chronic liver disease, were infected before the age of 35, and have no history of significant alcohol

use, are at extremely low risk of severe liver disease. Most of these persons, when biopsied, have normal liver histology or minimal fibrosis and are deemed "slow progressors." Slow progressors advance only one Metavir stage in 15-20 years or more. Women who are slow progressors are especially unlikely to develop severe liver disease during their lifetime.

Deferring liver biopsy is reasonable for inmates with persistently normal ALT levels when the risk of liver disease is extremely low. Chronic HCV infection should still be confirmed in such cases with a quantitative HCV RNA test, and if negative, should be repeated with a qualitative nucleic acid test to diagnose resolved HCV infection. Inmates with confirmed HCV infection and normal ALT levels should be monitored with a targeted history and physical examination every 6-12 months, along with a platelet count, AST, ALT, alkaline phosphatase and prothrombin time measurements.

A decreased platelet count, an increase in the AST/ALT ratio, and a prolonged prothrombin time are the earliest indicators of cirrhosis and portal hypertension and warrant an aggressive evaluation for liver disease.

- **Genotypes 2 and 3**: Liver biopsy can be deferred and antiviral therapy empirically initiated for certain inmates with genotypes 2 and 3 due to the high response rates to treatment for these patients. All inmates with HCV genotypes 2 or 3, however, should be advised of the potential toxicity of interferon and ribavirin and offered liver biopsy to help determine the urgency of therapy. Other inmates, with relative contraindications to antiviral therapy, or in whom other causes of liver disease are suspected, or who have evidence of severe liver disease on physical examination or laboratory testing, should have a liver biopsy to help guide treatment decision-making.

- **Genotypes 1, 4, 5, and 6:** Liver biopsy is generally indicated for all inmates with these genotypes, since treatment is less effective in these patients. Treatment without liver biopsy may be considered for inmates with suspected compensated cirrhosis, or with certain extrahepatic manifestations of HCV infection.

- **HIV co-infection:** Inmates with hepatitis C and HIV co-infection should receive a liver biopsy regardless of ALT levels or genotype, due to the increased risk of accelerated fibrosis and the greater potential for adverse reactions with antiviral therapy.

- **Compensated cirrhosis:** Inmates with compensated cirrhosis, that is suspected from clinical and laboratory parameters, should be either referred directly for liver biopsy or treated empirically with antiviral therapy (without biopsy confirmation) in consultation with a specialist.

- **Rebiopsies**: Inmates with normal liver histology or minimal fibrosis should be rebiopsied every 2-5 years. The timing of follow-up should be made on a case-by-case basis. Inmates with minimal fibrosis, but with marked hepatocellular necrosis and inflammation should be

rebiopsied in one year or referred for treatment on a case-by-case basis, since these inmates are at greater risk of developing progressive fibrosis.

Indications for antiviral therapy: Inmates with the following criteria are priority candidates for antiviral therapy based on evidenced-based data and the American Association for the Study of Liver Diseases (AASLD) recommendations:

- abnormal serum ALT values;
- liver biopsy with chronic hepatitis with significant fibrosis (more than portal fibrosis: Metavir ≥ stage 2 or Ishak ≥ stage 3);
- compensated liver disease (total bilirubin < 1.5 g/dL; INR < 1.5; albumin > 3.4 g/dL; platelet count > 75,000/mm^3; and no evidence of hepatic encephalopathy or ascites;
- acceptable pre-treatment labs: hemoglobin > 13 g/dL in men or > 12 g/dL in women; absolute neutrophil count > 1500/mm^3; creatinine < 1.5 mg/dL; and
- inmate is willing to be treated and conform to treatment requirements, including abstinence from alcohol and illicit drugs.

Hepatitis C treatment should be deferred in inmates with early hepatic fibrosis who have relative contraindications to antiviral therapy, until these complicating conditions are resolved. Conversely, antiviral therapy should be considered in inmates with stage 3 or 4 fibrosis despite the presence of relative contraindications. If treatment is pursued for such individuals, the inmate must be counseled on the increased risk of side effects, and/or the potential for exacerbations in medical or psychiatric illnesses.

Pretreatment evaluation: Inmates should be evaluated by a physician and screened for other medical conditions that may complicate antiviral therapy.

- **Screening tests:** The following tests should be obtained (unless completed recently):
  - **Serum chemistries:** Obtain liver enzymes, bilirubin, CBC with differential and platelet count, prothrombin time, TSH, renal function, anti-HIV, HBsAg, ferritin, ANA, fundoscopy for inmates with diabetes or hypertension, and other patient-specific diagnostic tests as medically indicated.
  - **Pregnancy test** for all female inmates: Ribavirin may cause fetal abnormalities. All female inmates of childbearing potential must have a pregnancy test immediately prior to initiating therapy.
  - **Cardiac risk assessment:** Inmates should have a basic cardiac risk assessment from a clinician, since hemolysis from ribavirin may precipitate angina pectoris. An electrocardiogram should be obtained in inmates with preexisting cardiac disease. Symptomatic inmates should be carefully evaluated for cardiac disease prior to initiating treatment.

- **Mental health evaluation:** A mental health evaluation should be performed by a psychiatrist or a psychologist before prescribing interferon and ribavirin therapy to determine if mental health treatment is warranted prior to antiviral therapy or if ongoing mental health assessments are needed during treatment.

  - The evaluation should include an assessment of axis I and axis II diagnoses, including a comprehensive alcohol and substance abuse history, and a suicide risk assessment. Interferon therapy has been associated with changes in mood and affect in most individuals. In a small percentage, significant depression, suicide attempts and completed suicides have resulted. The absence of a history of depression or suicide attempts does not appear to lessen the risk of these side effects from interferon; however, their presence should prompt heightened vigilance on the part of the treating providers.
  - Other mental illnesses or conditions, if not treated or not in remission, may adversely affect the inmate's ability to successfully complete a course of antiviral treatment, either due to issues of compliance or inability to tolerate even mild side effects.

- **Inmates with compensated cirrhosis:** Inmates with suspected or biopsy-confirmed compensated cirrhosis should have an upper endoscopy screening for esophageal varices, a liver ultrasound or abdominal CT-scan, and measurements of alpha-fetoprotein and ammonia prior to treatment initiation. If HCC or decompensated cirrhosis is diagnosed, antiviral therapy is contraindicated.

Treatment options: Pegylated interferon (alfa 2a or alfa 2b) plus ribavirin is the preferred drug regimen for treating chronic hepatitis C in the absence of contraindications to either drug. Pegylated interferon is available in two formulations: PEG-Intron® (alfa 2b) and Pegasys® (alfa 2a). Ribavirin is available as: Rebetol®, Copegus®, and generic preparations that are considered bioequivalent. Clinical studies have paired pegylated interferon alfa 2a with Copegus®; and pegylated interferon alfa 2b with Rebetol®. **Ribavirin is completely ineffective as monotherapy and should never be prescribed without interferon.**

Either a 12 or 24-week course of pegylated interferon and ribavirin is effective for patients with genotypes 2 or 3 depending on treatment response; whereas a 48-week course of treatment is recommended for patients with genotype 1. Patients with genotype 1 require higher doses of ribavirin. The optimal duration of antiviral therapy is unknown for persons with genotypes 4, 5, 6, or nontypable HCV; therefore, these patients should be treated with the 48-week course of treatment recommended for genotype 1 patients. Inmates who have contraindications to ribavirin, regardless of genotype, should be treated with a 48-week course of pegylated interferon alone.

Detailed drug dosages, monitoring parameters, and potential side effects are outlined in *Appendices 10a-10d (Antiviral Medications for Chronic Hepatitis C).*

Interferon/ribavirin side effects and adverse reactions: Inmates treated for chronic hepatitis C should be counseled by a clinician before and during treatment regarding both the anticipated and potential side effects/adverse reactions of interferon and ribavirin.

- **Interferon:** An influenza-like reaction often occurs within 6-8 hours of initial treatment with interferon. The fatigue, headache, fever, and myalgias often abate with subsequent treatments and can be partially aborted by premedication with antipyretics. Acetaminophen can be given safely up to 2 gm/day in divided doses. Nonsteroidal anti-inflammatory agents (NSAIDs) should not be prescribed.

  Chronic side effects of interferon can include severe fatigue, weight loss, reversible alopecia, irritability, rage, confusion, and neuropsychiatric disorders. Severe and incapacitating depression can occur, even in persons without previous histories of depression. Bone marrow suppression resulting in neutropenia and thrombocytopenia are potentially serious effects of interferon that should be anticipated and monitored closely, particularly in patients with cirrhosis or HIV infection. Thyroid dysfunction occurs in approximately 4% of persons treated with interferon and may result in irreversible thyroid dysfunction, even with cessation of drug therapy. Resultant hypothyroidism can be treated on a case-by-case basis with hormone replacement therapy, while continuing interferon; whereas, hyperthryoidism usually necessitates discontinuation of interferon.

  Pegylated interferons generally have similar side effect profiles compared to standard interferons; however, pegylated interferons induce neutropenia to a greater degree. Inmates with side effects to interferon should have their dosage reduced or therapy discontinued depending on the severity of the side effects. Serious sequelae may occur in less than 1% of persons receiving interferon treatment and can include: renal failure, pneumonitis, severe bone marrow suppression, visual and hearing loss, retinal hemorrhage, acute psychosis, and suicide.

- **Ribavirin:** Ribavirin causes a dose-related red cell hemolysis to variable degrees in nearly all persons who are treated. A decrease in the hemoglobin of 2-3 gm/dL and a decrease in hematocrit of 5-10% should be anticipated. Persons with a preexisting hemolysis or severe anemia (hemoglobin < 11 g or hematocrit $< 33\%$) or underlying cardiovascular or cerebrovascular disease should not receive ribavirin. Persons with HIV infection or other co-morbid conditions should be monitored closely. Anemia ordinarily develops between 1 and 4 weeks of initiating therapy. New onset of episodic chest pain during therapy should be presumed to be angina pectoris until proven otherwise. Symptoms of sudden hemolysis such as dyspnea, fatigue, headache, and palpitations may develop. If anemia occurs ribavirin should be reduced in dosage or discontinued.

  Clearance of ribavirin is significantly impaired in renal insufficiency; thus, the risk of adverse effects, particularly hemolytic anemia, increase significantly with a decline in renal function. Ribavirin dose should be reduced with impaired renal function (creatinine > 1.5 mg/dL), and ribavirin is contraindicated if the creatinine is > 2.0 mg/dL, or the creatinine clearance is < 50 ml/min. Ribavirin is absolutely contraindicated in dialysis patients, since

it is not dialyzable. Ribavirin also causes histamine-like side effects such as nasal stuffiness, itching, and skin irritations. More severe effects can include an asthma-like syndrome or bronchitis.

> **Ribavirin may cause fetal abnormalities. All female inmates of childbearing potential must have a pregnancy test prior to initiating therapy. Both women AND men must be counseled to use adequate birth control during treatment and for 6 months after treatment is completed.** Counseling of both women AND men regarding the risk of birth defects is particularly important for inmates awaiting release and receiving ribavirin or who have recently completed treatment.

Monitoring treated inmates: Inmates receiving interferon and ribavirin should be monitored as follows:

- **Clinician evaluations:** Clinician evaluations should occur weekly for one month, then monthly thereafter, to assess drug side effects and potential complications. Inmates with compensated cirrhosis, HIV infection, and other co-morbid conditions require more frequent monitoring, as do patients who develop significant side effects or complications while on therapy. Psychiatry and psychology consultations should be provided as clinically indicated while inmates are taking interferon.

- **Laboratory monitoring:** Inmates receiving interferon and ribavirin therapy should be monitored for drug toxicities in accordance with the following general guidance:

  - ALT at weeks 1, 2, and 4, and at 8-12 week intervals thereafter;
    (An unusual but serious complication of interferon or interferon and ribavirin combination therapy is the paradoxical worsening of hepatitis. If ALT levels increase significantly, antiviral therapy should be discontinued, ALT levels should be monitored closely, and the inmate should be monitored for signs and symptoms of hepatitis.)
  - Periodic bilirubin, prothrombin time, and serum chemistries, including creatinine/BUN repeated with any new elevations in ALT or symptoms or signs of liver disease;
  - CBC with differential/platelet count at weeks 1, 2, and 4, and at 4-8 week intervals thereafter; and
  - Thyroid function studies every 3 months during interferon therapy.

Treatment duration and maintenance: The recommended duration of interferon and ribavirin antiviral therapy and the assessment of treatment response varies with HCV genotypes and is assessed by the clearance of HCV RNA. An early viral response (EVR) is indicated by a 2 log decrease in viral load after 4-12 weeks of treatment. A sustained viral response (SVR) is indicated by the absence of detectable HCV RNA in the serum measured by a nucleic acid test 24 weeks after completion of antiviral therapy.

- **Genotypes 1, 4, 5, and 6:** Antiviral therapy for hepatitis C is administered for 12 weeks for inmates with HCV genotypes 1, 4, 5, or 6, followed by the measurement of quantitative

HCV RNA. A detected EVR in persons infected with HCV genotype 1, predicts a sustained viral response (SVR). Inmates with an EVR should be treated for another 36 weeks (total 48 weeks course of treatment). (Use the same laboratory and same type of viral load testing when comparing pretreatment and post-treatment levels of HCV RNA.) Failure to achieve an EVR (not suppressing HCV RNA by at least two logs from baseline) predicts treatment failure. **Antiviral therapy should be discontinued in these patients after 12 weeks of treatment.** In the absence of evidenced-based data on treatment response for persons infected with HCV genotypes 4, 5, and 6, inmates with these genotypes should be treated like those with HCV genotype 1.

- **Genotypes 2 and 3:** Patients infected with HCV genotypes 2 or 3 may be effectively treated with 12-24 weeks of therapy. Achieving an SVR after 12 weeks of treatment has the following potential benefits: a decreased duration and severity of medication side effects, lower overall treatment costs, and increasing the number of inmates who could complete antiviral therapy prior to release. The following two options should be considered:

  - **Option 1**
    - Administer antiviral therapy for 4 weeks (pegylated interferon alfa 2a or 2b with ribavirin)
    - Check HCV RNA after 4 weeks of treatment. If undetectable or ≥ 2 log decrease from baseline, complete a total of 12 weeks of treatment
    - Confirm that HCV RNA is undetectable at 12 weeks, and again at 6 months post-treatment.
      - If HCV RNA has not shown a ≥2 log decrease at 4 weeks, check the viral load again at 12 weeks.
      - Complete 24 weeks of treatment if HCV RNA is undetectable or ≥ 2 log decrease from baseline.
      - Discontinue treatment (nonresponder) if HCV RNA has not shown a ≥ 2 log decrease at 12 weeks.

    (In clinical trials, relapse rates were slightly higher in the 12 week vs. 24 week treatment groups. If relapse is detected after a 12 week course of treatment, the same regimen of peg-interferon and ribavirin should be continued for a full 24 weeks.)

  - **Option 2**
    - Administer antiviral therapy for 12 weeks.
    - Check HCV RNA after 12 weeks of treatment.
      - Complete 24 weeks of treatment if HCV RNA is undetectable or ≥2 log decrease from baseline and confirm that HCV RNA is undetectable 6-months post-treatment.
      - Discontinue treatment (nonresponder) if HCV RNA has not shown a ≥2 log decrease at 12 weeks.

Managing anemia and neutropenia: The impact of early versus late antiviral dosage reductions and the degree of dose reductions on sustained virologic response has been

evaluated in clinical trials. A significant reduction in SVR was only observed in patients who required a reduction in the dose of ribavirin to less than 60 percent of the originally prescribed dose within the first 20 weeks of therapy. Reducing the dose of peginterferon during the first 20 weeks of treatment had no significant impact on SVR. Furthermore, reducing the dose of either peginterferon or ribavirin, even to less than 60 percent of the original dose, after 20 weeks of treatment, when patients had undetectable HCV RNA, had no effect on the SVR.

The routine use of erythropoietin or granulocyte colony-stimulating factor (G-CSF) to treat anemia and neutropenia and therefore avoid or ameliorate the need for dose reduction of peginterferon and ribavirin is not recommended due to the lack of definitive indications. Use of these agents may be approved on a case-by-case basis in consultation with a Central Office physician, based on individual patient characteristics and evidence of an early viral response (EVR) to treatment. Neither of these agents will correct interferon-induced thrombocytopenia; therefore, dose reduction or discontinuation is essential when platelet counts drop to potentially dangerous levels. (Recombinant thrombopoietin cannot yet be recommended, due to lack of safety and efficacy data.)

Re-treatment: Patients who do not achieve a SVR following antiviral therapy can be categorized as nonresponders or relapsers.

- **Nonresponders:** These patients do not adequately respond to antiviral therapy by either:
  1) developing a SVR upon the completion of antiviral therapy; or by
  2) clearing viremia at a rate that predicts a SVR if treatment were continued.

- **Relapsers:** These patients have undetectable levels of HCV RNA at the end of treatment, but do not attain a SVR, i.e., HCV RNA is detectable by 24 weeks after completion of initially effective antiviral therapy.

Re-treatment of relapsers and nonresponders should be considered on a case-by-case basis with the approval of Central Office HSD, while considering the following:

- **Relapsers should not be retreated with the same regimen.** Although direct comparison studies have not been performed between the two brands of pegylated interferon, they are considered to be equivalent. Therefore, a treatment relapser after a course of one pegylated interferon preparation (plus ribavirin) would not necessarily be retreated with the other brand of pegylated interferon.

- **Re-treatment should be considered for those inmates who are most likely to benefit from therapy and are at significant risk of disease progression** by weighing the follow factors in combination:

  - the severity of underlying liver disease determined by liver biopsy;
  - the viral genotype and other predictive factors that influence response rates;
  - the previous regimen and the relative potency of the new regimen (e.g., non-pegylated interferon, interferon monotherapy); and

- the previous response to therapy.

- **Nonresponders to a standard pegylated interferon and ribavirin regimen will not be retreated.**

- **Long-term antiviral maintenance therapy should not be prescribed** because it is still investigational and has unproven benefits.

Complicating medical conditions:

- **Renal insufficiency**: Persons with HCV infection have an increased risk of renal disease that is often associated with cryoglobulinemia, and histologic findings that resemble idiopathic membranoproliferative glomerulonephritis (MPGN). Clinical manifestations include hematuria, proteinuria that is often in the nephrotic range, and a variable degree of renal insufficiency. In the absence of liver disease that warrants antiviral therapy for HCV infection, inmates with moderate to severe kidney disease (e.g., nephrotic syndrome, elevated plasma creatinine concentration, new hypertension, fibrosis or tubulointerstitial disease on biopsy) should still be considered for antiviral therapy for HCV infection. Specific treatment regimens should be individualized in consultation with a Central Office physician and available physician experts.

- **Hemodialysis:** The goal of treating hepatitis C in persons with end-stage renal disease is to reduce the progression of liver disease and/or clear the HCV infection in patients who may later undergo renal transplantation. Evaluation of these patients is complicated by several factors: (1) ALT levels are more likely to be normal or near-normal in hemodialysis patients, even in the presence of significant fibrosis; (2) the need for a liver biopsy must be balanced against the increased risk of severe bleeding; and (3) since interferon is contraindicated after renal transplantation, hepatitis C treatment should be considered prior to referring the inmate for transplant consideration. *For dialyzed patients*, the recommended dose of pegylated interferon 2a is 135 μg administered subcutaneously, as monotherapy.

- **HBV and HCV co-infections:** Antiviral therapy for inmates with HBV and HCV co-infections should be initiated with great caution, and only in consultation with a specialist, due to the uncertainty of the risks and benefits of treatment and lack of a recommended treatment regimen. All cases which may be candidates for treatment should be reviewed with a Central Office physician.

- **HIV and HCV co-infections:** Pegylated interferon and ribavirin therapy should be considered for all inmates with chronic hepatitis C and HIV co-infection, since HIV increases the risk of hepatic fibrosis and end-stage liver disease. Treatment response rates, however, are lower in HIV infected patients and the risk of serious adverse effects are greater. **The recommended duration of treatment, assuming an EVR at 12 weeks, is 48 weeks of therapy, regardless of genotype**. The following treatment considerations should also be noted for inmates with HCV/HIV co-infections:

- Treatment for HIV and HCV infections should not be initiated simultaneously.
- Inmates who have not been treated for either HIV infection or chronic hepatitis C should first be treated with antiretroviral therapy if the inmate is a candidate for treatment (AIDS or CD4+ T-cell count < 350 cells/mm^3); otherwise consider antiviral therapy for chronic hepatitis C in inmates with documented liver disease.
- Patients with HIV infection are at greater risk of hepatotoxicity with interferon/ribavirin therapy, particularly if they are on a HAART regimen. Ritonavir and nevirapine have been specifically implicated in some studies, although other studies suggest an increased risk with any HAART regimen. ALT levels should be monitored every 1-2 months while on therapy.
- Didanosine (ddI) should not be co-administered with either interferon or ribavirin due to the increased risk of pancreatitis and lactic acidosis.
- Bone marrow suppression from HIV infection or antiretrovirals, such as zidovudine (AZT) may complicate treatment for hepatitis C. In order to avoid severe anemia from ribavirin-induced hemolysis, erythropoietin therapy or an alternative HAART regimen may be warranted.

- **Latent TB and chronic HCV infection:** Inmates with latent TB infection and chronic HCV infection should be considered for isoniazid treatment and should be monitored for hepatotoxicity in accordance with the same guidelines established for patients without HCV infection. All inmates require screening for symptoms of hepatitis while taking isoniazid. Those inmates with baseline ALT elevations, also warrant periodic monitoring of ALT levels. *Isoniazid should be discontinued in inmates with marked elevations in ALT levels* or significant signs or symptoms of hepatitis in accordance with BOP Guidelines for the Management of Tuberculosis.

Infection Control

Patient education: All inmates should be counseled during orientation to the institution and when appropriate during clinical evaluations of the importance of preventing blood exposures to others during activities of daily living such as sharing toothbrushes and razors and through unsafe behaviors such as injection drug use, tattooing, and sexual contact with other inmates.

Reporting: Each institution should have a surveillance system for notifiable infectious diseases in accordance with BOP policy. Acute hepatitis C is a reportable condition in many states. *Inmates with acute hepatitis C should be reported to local or state authorities where* required and to the Central Office HSD. Inmates with chronic HCV infection should be reported to the local or state health authorities where required.

Containment: Inmates with acute hepatitis C and chronic HCV infection do not require isolation, but should be counseled on the specific measures necessary for preventing further transmission of HCV to others during incarceration and upon release and should be managed while incarcerated using standard infection control precautions. Non-disposable patient-care items must be appropriately cleaned, disinfected, or sterilized based on the use; and measures

must taken to prevent cross contamination during patient care, e.g., dialysis, vascular access, cauterizing, dental procedures, etc., in accordance with CDC guidelines.

Hemodialysis:

- **Screening:** Inmates on hemodialysis without chronic HCV infection should have serum ALT levels measured monthly and anti-HCV measured by an immunoassay semi-annually to screen for newly acquired HCV infection. All inmates receiving hemodialysis with a positive anti-HCV screening immunoassay should have a supplemental qualitative HCV RNA performed.

- **Infection control:** Infection control measures to reduce HCV transmission during hemodialysis should be implemented in accordance with CDC guidelines. Inmates with HCV infection receiving dialysis do not need to be isolated from other patients or dialyzed separately on dedicated machines. Dialyzers used for inmates with HCV infection can be reused.

Contact investigation: Contact investigations should be initiated for those inmates with acute hepatitis C who have been incarcerated during the 2 weeks to 6 months prior to disease onset. A contact investigation tool is attached in *Appendix 11a (Contact Investigation - Acute Hepatitis C)* and *Appendix 11b (Line Listing - Acute Hepatitis C)* In addition to documenting medical visits or procedures during which the inmate may have had blood exposure, inmates should be interviewed for information regarding recent drug injection, tattooing or body piercing and sexual contacts. Enhanced case-finding, and counseling and testing for anti-HCV, should be initiated for sexual contacts, injection partners and those who have used the same tattooing equipment.

Post-exposure Management:

- **Emergent care:** Wounds and skin sites that have been in contact with blood or bloody body fluids should be washed with soap and water. Exposed mucous membranes should be flushed with water. Squeezing the wound and treating with topical antiseptics are not recommended.

- **Counseling:** Inmates with percutaneous or mucosal exposures to blood should be assessed by a qualified health care provider and counseled regarding their risk of acquiring HCV infection, the natural history of HCV infection, and the recommendations for post-exposure management.

- **Post-exposure follow-up:** No vaccine or passive immunization is available to prevent acquisition of HCV infection following an exposure. The following guidelines should be used for managing inmate exposures to HCV:

  - Whenever feasible, the source of the exposure should be tested for anti-HCV, unless the source's infection status is already known.

- Exposed inmates should be referred for medical evaluation and follow-up.
- Measure anti-HCV by a screening immunoassay (confirmed by HCV RNA, if positive) in the exposed inmate immediately after exposure and at week 12.
- Measure HCV RNA by a qualitative nucleic acid test, and ALT levels in the exposed inmate immediately after exposure, at week 4, and at week 12.
- Inmates with evidence of newly acquired HCV infection should be appropriately counseled and referred for further medical evaluation including possible treatment for acute hepatitis C.

5. Hepatitis D Virus (HDV)

Transmission

HDV is a defective RNA virus that requires HBsAg for structural integrity and replication. HDV, also known as hepatitis delta virus, is transmitted through percutaneous exposures to blood such as through injection drug usage. Sexual transmission occurs, but is much less efficient than for HBV. Perinatal transmission is rare. Inmates at highest risk for delta hepatitis have a history of injection drug use or have resided in areas of the world with a high prevalence of infection such as Turkey, Egypt, Southern Italy, Spain, Russia, Romania, and the Amazon River Basin.

Natural History and Diagnosis

Natural history: Acute HBV-HDV co-infection (concurrent infections with HBV and HDV) results in a severe acute hepatitis more frequently than infection with HBV alone, but progression to chronic infection is uncommon. HBV-HDV superinfection (HDV infection acquired in a person with preexisting chronic HBV infection) results in chronic HDV infection and a higher risk for cirrhosis and hepatocellular carcinoma compared to persons infected with HBV alone.

Diagnosis: Serologic detection of HDV infection varies depending on whether the virus is acquired through co-infection or superinfection. Following HBV-HDV co-infection both IgM anti-HDV and IgG anti-HDV are detectable. IgM anti-HDV is more likely to be detectable during the acute illness; whereas IgG anti-HDV is more like to be present during convalescence, but there is considerable overlap. Chronic infection is uncommon. IgG anti-HDV is usually undetectable with the disappearance of HBsAg and HDAg. Following HBV-HDV superinfection, chronic HDV infection with detectable HDAg usually occurs. Both IgM anti-HDV and IgG anti-HDV remain detectable.

Treatment

The treatment of acute delta hepatitis is supportive similar to that for acute hepatitis B. Periodic clinician evaluations should be conducted for inmates with chronic HDV infection in

accordance with guidelines for monitoring chronic HBV infection. Inmates with chronic delta hepatitis should be considered candidates for antiviral therapy using the same criteria as inmates with chronic HBV infection. Antiviral therapy for delta hepatitis should be considered in consultation with a specialist. Treatment regimens may differ from those recommended for persons infected with HBV alone.

Infection Control

Patient education: All inmates should be counseled during orientation to the institution and when appropriate during clinical evaluations of the importance of preventing blood exposures to others during activities of daily living such as sharing toothbrushes and razors and through unsafe behaviors such as injection drug use, tattooing, and sexual contact with other inmates.

Reporting: Inmates with acute delta hepatitis should be reported to state and local health authorities as required. Acute delta hepatitis cases should also be reported to the Central Office HSD.

Containment: Inmates with acute delta hepatitis or chronic HDV infection do not require isolation, but should be counseled on the specific measures necessary for preventing further transmission of HDV to others during incarceration and upon release and should be managed while incarcerated using standard infection control precautions. Non-disposable patient-care items must be appropriately cleaned, disinfected, or sterilized based on the use; and measures must be taken to prevent cross contamination during patient care, e.g., dialysis, vascular access, cauterizing, dental procedures, etc., in accordance with CDC guidelines.

Hemodialysis: Routine testing for HDV infection for inmates receiving hemodialysis is not recommended. Inmates who are known to be infected with HDV should be isolated from all other dialysis patients, especially those who are HBsAg-positive.

Contact investigation: A contact investigation should be conducted for all inmates diagnosed with acute delta hepatitis using a similar approach to that recommended for acute hepatitis C cases (i.e., evaluating potential percutaneous exposures, such as injection drug use or tattooing). Suspected contacts should be tested for HBsAg in order to identify at-risk persons with chronic HBV infection (HBsAg-positive).

Post-exposure management: Wounds and skin sites that have been in contact with blood or body fluids should be washed with soap and water. Exposed mucous membranes should be flushed with water. Squeezing the wound or treating with antiseptics is not recommended. Prophylaxis for acute HBV infection should be provided to susceptible contacts. HDV can not infect an individual if infection with HBV is prevented with hepatitis B immunoglobulin or hepatitis B vaccine. Inmate contacts with chronic HBV infection should be counseled on the risk for HBV-HDV superinfection.

6. Cirrhosis

Transplantation Issues

Liver transplantation is the treatment of choice for patients with hepatic failure from chronic HBV and HCV infections; however due to the lack of available donor organs this option is limited, not only for inmate populations, but also for persons in the community. Split liver transplantation from living donors is a promising option that may expand transplantation options to patients with liver failure in the foreseeable future. Even with available donor livers, transplantation may be unsuccessful for patients with end-stage liver disease from HBV and HCV infections, due to high rates of re-infection and progressive liver disease in the transplanted organ.

Nevertheless, inmates with hepatic failure from viral hepatitis should be assessed on a case-by-case basis for eligibility for liver transplantation by assessing patient specific factors such as the following: MELD scores that help predict patient mortality, medical contraindications for transplantation, mental health stability, evidence of ongoing substance abuse, criminal history factors that may negate successful transplantation, and patient motivation (as evidenced by adherence to current treatment recommendations). Inmates who are potential candidates for liver transplantation should be advised of the limited access to donor livers and, where available, be referred for evaluations to local transplant centers. If transplantation during incarceration is not feasible, inmates should be evaluated for early release while considering public safety concerns, local correctional policies, and governing laws and regulations.

Morbidity Assessment

The Model for End-stage Liver Disease (MELD) predicts liver disease severity and the risk of three month mortality based on serum creatinine, serum total bilirubin, and prothrombin time (INR). In a recent study of patients with end-stage liver disease awaiting liver transplantation, 3 month mortality varied with increasing MELD scores: MELD < 9, mortality was 1.9%; MELD of 20-29, mortality was 19.6%, MELD of 30-39, mortality was 52.6%; and MELD ≥ 40, mortality was 71.3%.

The value of MELD as a predictor of mortality is limited by its dependency on serum creatinine which can fluctuate with changes in fluid status. MELD is a better predictor of mortality for different populations than of death for any given individual. Nevertheless, MELD provides useful information for assessing the morbidity of inmates with end-stage liver disease.

All inmates with decompensated cirrhosis should have a MELD score determined to assess mortality risk. MELD scores should be recalculated over several weeks in inmates with shifting fluid status.

The MELD score can be calculated by utilizing a calculator provided by United Network for Organ Sharing available at http://www.unos.org/resources/MeldPeldCalculator.asp?index=98 Data required includes: date of birth, bilirubin, creatinine, INR and dialysis status.

Inmates with MELD scores of 30 or greater should be considered for Medical Referral Center designation. (The MELD score predicts mortality independent of clinical parameters such as hepatic encephalopathy, ascites, and variceal bleeding. These significant complications of cirrhosis, however, should also be considered in referring patients for Medical Referral Center designation.)

Preventive Measures

The following preventive measures should be considered for inmates with cirrhosis:

- **Immunize** against influenza (annually), pneumococcal pneumonia, and hepatitis A and B (unless immune).

- **Provide patient education** on:

  - selecting a low-salt, low fat, "heart healthy" diet;
  - complete abstinence of alcohol during incarceration and after release; and
  - avoidance of iron supplements and potentially hepatotoxic medications, such as nonsteroidal inflammatory drugs (NSAIDS).

- **Perform baseline endoscopy** to screen for esophageal varices. (Follow-up annual screening can be considered on a case-by-case basis, but the benefit of repeated screening is unclear. Once esophageal varices have been identified the risk of future variceal hemorrhage is 25-35%.)

- **Prescribe nonselective beta-blocker therapy, such as propranolol or nadolol, for inmates with large esophageal varices or red wale markings on endoscopy.** (The dose of beta-blocker should be titrated weekly to reduce the resting heart rate by 25%, but not less than 55 beats/minute or reducing the systolic blood pressure to lower than 90 mm Hg.) Long-acting nitrates can be added to nonselective beta-blockers in patients who do not respond to beta-blockers alone, but long-acting nitrates should not be used alone.

- **Provide primary prophylaxis for spontaneous bacterial peritonitis** (SBP) with an antibiotic, such as ciprofloxacin (generally limit to short treatment periods in high risk patients such as those with upper gastrointestinal hemorrhage).

- **Periodically screen for HCC** by ultrasonography (e.g., annually) **and alpha-fetoprotein testing** (e.g. semiannually), but note, the optimal screening strategy is uncertain.

Definitions

General Definitions

Absolute contraindication is a condition or factor that in and of itself ordinarily precludes a specific intervention.

Relative contraindication is a condition or factor that may preclude a specific intervention when considered in conjunction with other criteria.

Qualitative viral assay is a nucleic acid test (NAT) used to detect the presence, but not the amount of virus present.

Quantitative viral assay is a nucleic acid test (NAT) used to measure the amount of virus present.

Standard precautions are protective measures used for all patient/inmate contacts and situations to prevent the spread of infections transmitted by contaminated blood and body fluids. Precautions include the wearing of gloves and other personal protective equipment (personal protective equipment should be an impervious barrier) when soiling is likely; and procedures for protective handling (handling includes the use of puncture-resistant devices and leak-proof protection) of contaminated materials and equipment, and routine cleaning of all contaminated surfaces and equipment.

Hepatitis A

Hepatitis A is an acute viral hepatitis caused by a highly infectious RNA virus that is transmitted primarily by the fecal-oral route and close personal contact. Acute hepatitis A has a mild to fulminant clinical presentation that resolves without progression to chronic infection or chronic hepatitis.

HAV is hepatitis A virus, an enveloped RNA virus.

IgM anti-HAV is the antibody subclass to HAV that develops with acute infection. False positive IgM anti-HAV serologies can occur.

IgG anti-HAV are antibodies to HAV that confer immunity.

Total anti-HAV are total antibodies to HAV that include IgG and IgM antibody subclasses.

Hepatitis B

Hepatitis B is an acute or chronic viral hepatitis caused by a DNA virus that is transmitted primarily through sexual contact, exposures to blood, and perinatally.

HBV is hepatitis B virus, a double-stranded DNA virus.

HBsAg is hepatitis B surface antigen, a viral envelope antigen that is detectable during acute or chronic HBV infection.

HBeAg is hepatitis e antigen, a secreted, viral antigen of the hepatitis B viral core that is indicative of active viral replication and increased infectiousness.

Anti-HBs is the antibody to hepatitis B surface antigen that confers immunity to HBV infection. Anti-HBs is usually detectable after infection with HBV and following vaccination.

IgM anti-HBc is the antibody to hepatitis B core antigen that develops with acute HBV infection.

Total anti-HBc is the total antibody response to hepatitis B core antigen that is detectable after acute HBV infection and remains detectable during convalescence. Measurement of total anti-HBc is a useful screen for past HBV infection. Total anti-HBc is not detectable following hepatitis B vaccination.

Anti-HBe is the antibody to hepatitis e antigen that develops as viral replication and active hepatitis B begin to wane. Development of anti-HBe coincides with the loss of HBe antigen.

Hepatitis C

Hepatitis C is an acute or chronic viral hepatitis caused by an RNA virus that is transmitted primarily by percutaneous contact with blood.

HCV is hepatitis C virus, an enveloped, single-stranded RNA virus.

Anti-HCV is the antibody to HCV core and nonstructural proteins that is detectable from several weeks to months after clinical hepatitis.

Anti-HCV screening assay is an immunoassay such as an enzyme immunoassay (EIA) or chemiluminescence immunoassay (CIA) used to screen for HCV infection by measuring antibodies to HCV antigens.

RIBA (anti-HCV) is the recombinant immunoblot assay that measures antibodies to HCV antigens through immunoblot technology.

Early viral response (EVR) after treatment of chronic hepatitis C with pegylated interferon and ribavirin is a minimum two log decrease in the level of HCV RNA after the first 12 weeks of treatment compared to pretreatment levels, as measured by a quantitative nucleic acid test (NAT).

Sustained viral response (SVR) after antiviral treatment of chronic hepatitis C is the absence of detectable HCV RNA in the serum 24 weeks after treatment is completed, measured by a qualitative NAT for HCV RNA with a lower limit of detection of 50 IU/ml or less.

Hepatitis D

HDV is hepatitis delta virus, a defective single-stranded RNA virus that requires HBV for structural integrity and replication.

Hepatitis D or delta hepatitis is an acute or chronic hepatitis caused by HDV.

HBV-HDV co-infection is the simultaneous infection of HBV and HDV.

HBV-HDV superinfection is acute HDV infection in a person with preexisting chronic HBV infection (HBsAg-positive).

HDAg is hepatitis delta antigen.

IgM anti-HDV is an antibody subclass to HDV.

IgG anti-HDV is an antibody subclass to HDV.

Cirrhosis

Compensated cirrhosis is defined as: total serum bilirubin less than 1.5 g/dL; international normalized ratio (INR) less than 1.5; albumin greater than 3.4 g/dL; platelet count greater than 75,000 k/mm^3; and no evidence of the following: ascites by liver ultrasound, esophageal varices by upper endoscopy, hepatic encephalopathy, or elevations in alfa-fetoprotein or serum ammonia.

Decompensated cirrhosis is cirrhosis of the liver with evidence of significant liver disease, such as ascites, encephalopathy, marked thrombocytopenia, bleeding esophageal varices; and loss of liver synthetic function, e.g., albumin < 3.5 g/dL, total bilirubin > 1.5 mg/dL and international normalized ratio (INR) > 1.5.)

MELD or Model for End-stage Liver Disease is a validated disease severity index that uses age, creatinine, bilirubin, and prothrombin time to predict mortality.

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Appendix 1a. Contact Investigation - Acute Hepatitis A

Inmate name: **Date of Report:** ___/___/_____

Inmate number: **Facility:** **Date/Facility entry:** ___/___/_____

Date symptom onset: ___/___/_____ **Date BOP entry:** ___/___/_____

Reported by (name and title):

Laboratory Test	Date	Result
IgM anti-HAV		
IgM anti-HBc		
HBsAg		
anti-HCV by ☐EIA ☐RNA ☐RIBA		

1. **Reported to local health department?** ☐Yes ___/___/___ ☐No (reason)

2. **In the 2-6 weeks prior to illness onset, was patient in a BOP facility?**
   ☐Yes (complete BOP investigation necessary)
   ☐No (local/state health department to do investigation - proceed to #7.

3. **Risk factors** (2-6 weeks prior to illness onset):
   a) Close contact with a person with confirmed/ suspected acute hepatitis A?
   ☐No ☐Yes: ☐sexual partner ☐cell mate ☐ dorm mate
   b) Illicit drug use? ☐Yes ☐No
   c) Sexual partners? ☐Yes (#____) ☐No
   d) Work assignments:

4. **Detection and prevention of common source outbreaks:**
   a) Employed in food services? ☐Yes ☐No
   (If yes, enhance case-finding among persons eating at location)
   b) Part of a recognized common-source foodborne outbreak? ☐Yes ☐No

5. **Vaccination history:** Vaccinated against hepatitis A? ☐No
   ☐Yes When: Dose #1 date:___/___/_____ Dose #1 date:___/___/_____

6. **Opportunities for prevention of this case:**
   Was patient a cell or dormitory mate of a person with acute hepatitis? ☐Yes ☐No

7. **Contact evaluation for post-exposure prophylaxis:** Susceptible inmate contacts should ordinarily receive immunoglobulin (IG prophylaxis, 0.02 mL/kg IM in the deltoid or gluteal muscle) to prevent acute HAV infection within 2 weeks of exposure.
   Consult with local or state health department prior to administration.

8. **Susceptible contacts include:** cellmates, close personal contacts, injection drug use contacts, and sexual contacts. (Establish line listing.)

Appendix 1b. Line Listing - Acute Hepatitis A (Limited Official Use)

Close contacts: cell mates, sexual contacts, persons sharing toilet facilities, etc.

#	Contact Name	Registration #	Contact Type	Date IG given

Food Service (FS) Workers screened (screen food handlers[1] as potential source in every case)

#	Potential Source Name	Registration #	IgM anti-HAV[1]	Date IgG given[2]

[1] if symptomatic; [2] if index case is a foodhandler

If foodhandler[3] has acute hepatitis A: identify housing units/dorm/etc. with inmates eating food from location where foodhandler worked while ill and consider IG prophylaxis for inmates from these housing units (consult first with health department)

	Housing Unit /Dorm or other id'd area	Number	IG Given?

[3] **Foodhandler** = food service workers who prepare or touch the food before it is eaten.

Appendix 2. Inmate Fact Sheet: Hepatitis B and C Viral Infections

Am I at risk of infection with hepatitis B virus (HBV) or hepatitis C virus (HCV)?

You may be at risk for HBV or HCV infection if you have ever injected drugs or had sex with an infected partner. HBV is more easily transmitted through sex and from a mother to her child compared to HCV. Persons receiving blood transfusions prior to 1992 may be at risk for HCV infection. Talk to a health care provider about the risks of infection that affect you personally.

How can I prevent getting HCV or HBV while I am in prison?

- Do not have sex with other inmates, shoot drugs, or get a tattoo or body piercing.
- Do not share tooth brushes, razors, nail clipping devices, or other personal items that might have blood on them with other inmates.

Are these infections dangerous to my health?

Most persons infected with HBV or HCV do not develop serious problems. However, a small but significant number develop serious liver disease. Talk to a health care provider about your personal risks for developing liver disease.

Why should I be tested for HBV or HCV infection?

You should be tested if you are at risk so doctors can monitor your infection and assess your need for treatment now or in the future. You should also be tested so that you can better prevent others from getting infected, including your infant if you are pregnant.

How do I get tested for HBV or HCV?

A simple blood test can determine if you are infected.

How can I prevent giving HBV or HCV to others if I am already infected?

- First, remember that you can spread these infections even if you feel fine.
- Do not shoot drugs or have sex with other inmates.
- Do not share personal items that might have your blood on them, such as toothbrushes, dental appliances, nail-clipping equipment or razors.
- Cover your cuts and skin sores to keep your blood from contacting other persons.
- If you are being released, talk to a health care provider about specific ways you can reduce the risks of spreading HBV or HCV to others.

Appendix 3. Interpretation of Hepatitis B Virus Serologic Markers[1]

HBsAg	Total Anti-HBc	IgM Anti-HBc	Anti-HBs	Interpretation
-	-	-	-	**Susceptible (never infected)**
+	-	-	-	**Acute infection, early incubation[2]**
+	+	+	-	**Acute infection[3]**
-	+	+	-	**Acute resolving infection[3]**
-	+	-	+	**Past infection (recovered & immune)**
+	+	-	-	**Chronic infection**
-	+	-	-	**Multiple interpretations[4]**
-	-	-	+ ≥ 10 mIU/ml	**Immune from vaccination**

Abbreviations:

HBsAg	hepatitis B surface antigen
Total anti-HBc	total antibody to hepatitis B core antigen
IgM anti-HBc	immunoglubulin M antibody to hepatitis B core antigen
Anti-HBs	antibody to hepatitis B surface antigen

[1] Adapted from: CDC (2004). Interpretations of the Hepatitis B Panel. www.cdc.gov/ncidod/diseases/hepatitis/b/Bserology.htm.

[2] Note: Transient HBsAg positivity (lasting < 21 days) might be detected in some patients during vaccination.

[3] IgM usually wanes after 5 months post-infection, but may persist longer

[4] Multiple interpretations: may be recovering from acute HBV infection; may be distantly immune and test not sensitive enough to detect low level of anti-HBs in serum; may be susceptible with a false positive anti-HBc; or may be undetectable level of HBsAg present in the serum and the person is actually a carrier. Most persons positive for anti-HBc alone are unlikely to be infectious except in certain exposures involving very large amounts of blood.

Appendix 4. Antiviral Medications for Chronic Hepatitis B

Medication / Dosage	Baseline Tests / Monitoring	Adverse Reactions / Comments
Interferon alfa 2b (Intron A®) **Dose:** 5 million units SQ daily or 10 million units SC thrice (3 x) weekly **Pegylated interferon alfa 2a** (Pegasys®) **Dose:** 180 mcg SQ weekly For HBeAg-positive 16 to 24 weeks of treatment recommended HBeAg-negative 1-year or more of treatment recommended	**Baseline Tests:** ▸ anti-HIV, anti-HCV, anti-HDV ▸ HBeAg, HBV DNA ▸ ALT / AST, liver function ▸ CBC with differential and platelets ▸ chemistry panel ▸ *calculated creatinine clearance/* BUN ▸ thyroid function studies ▸ mental health assessment **Monitoring:** ▸ Clinician evaluations every week x 1 month then monthly ▸ CBC with differential and platelets ▸ ALT / liver function ▸ creatinine / BUN ▸ thyroid function studies ▸ psychology / psychiatry monitoring, as necessary	**Adverse Reactions:** ▸ fever, fatigue, myalgias ▸ nausea & diarrhea ▸ alopecia ▸ headache ▸ psychiatric (depression, anxiety, irritability) ▸ neutropenia and thrombocytopenia ▸ thyroid dysfunction ▸ renal failure ▸ injection site irritation **Comments:** ▸ contraindicated with decompensated cirrhosis ▸ Cost: high
Lamivudine (Epivir-HBV®) **Dose:** 100 mg orally, daily for one year or more (normal renal function and HIV seronegative) Recommended dose for HIV co-infection is 150 mg bid along with other anti-retroviral medications. Optimal treatment duration unknown. ***See warning below**	**Baseline tests and monitoring:** same as above except thyroid studies and mental health assessment only necessary if clinically indicated.	**Adverse Reactions:** ▸ lactic acidosis ▸ hepatomegaly **Comments:** *Lamivudine is less attractive* treatment option due to lack of long term efficacy and strong association with drug-resistant mutants. Do not combine with interferon or other antiviral agents for hepatitis B.

***Warning: Due to the risk of precipitating liver failure, do not discontinue lamivudine, entecavir or adefovir dipoxovil without consulting a physician expert.**

Appendix 4. Antiviral Medications for Chronic Hepatitis B (Page 2)

Medication / Dosage	Baseline Tests / Monitoring	Adverse Reactions / Comments
Adefovir dipivoxil *Hepsera®* **Dose:** 10 mg orally, daily Adjust for renal impairment Optimal treatment duration unknown. Treat for minimum of one year. ***See warning below**	**Baseline Tests:** *Same as above except thyroid studies and mental health assessment only necessary if clinically indicated.* **Monitoring:** ▸ ALT, liver function ▸ creatinine / BUN **(Discontinue if creatinine rises more than 0.5 above baseline)**	**Adverse Reactions:** ▸ lactic acidosis ▸ hepatomegaly **Comments:** ▸ Medications well tolerated and rate of developing drug resistance is low. ▸ Low level activity against HIV. ▸ Active against lamivudine resistant mutants
Entecavir Baraclude® **Dose:** ▸ 0.5 mg orally, daily in nucleoside-treatment-naive adults ▸ 1 mg orally, daily in lamivudine-refractory adults ▸ Adjust for renal impairment Optimal treatment duration unknown. Treat for minimum of one year. ***See warning below**	**Baseline Tests:** Same as above **Monitoring:** ▸ ALT, liver function function ▸ Clinical and laboratory follow up should continue for several months after treatment is stopped	**Adverse reactions:** ▸ lactic acidosis ▸ hepatomegaly **Comments:** ▸ Since entecavir is primarily eliminated by the kidneys, co-administration of drugs that reduce renal function or compete for active tubular secretion may increase serum concentrations of either entecavir or the co-administered drug. ▸ Effective against lamivudine resistant HBV mutants; activity against dual mutants is significantly less than that of wild-type HBV. ▸ Not active against HIV

***Warning: Due to the risk of precipitating liver failure, do not discontinue lamivudine, entecavir or adefovir dipoxovil without consulting a physician expert.**

Appendix 5. Viral Hepatitis Vaccine Doses and Schedules

Vaccine Type	Dose (mL)	Volume	# Doses in series	Schedule (months)
Hepatitis A and B Vaccines for Adults				
Hepatitis A				
Havrix[1]	1,440 EL.U[3,5]	1	2	0 and between 6 - 12
VAQTA[2]	50 U[5]	1	2	0 and between 6 - 12
Hepatitis B				
Recombivax-HB[2]	10 mcg[5]	1	3	0, 1, and 6
Engerix-B[1]	20 mcg[5]	1	3	0, 1, and 6
Hepatitis A and B combination				
Twinrix[1]	20 mcg (B)[5] 720 EL.U.(A)	1	3	0, 1, and 6
Source: Adapted from CDC guidelines, *MMWR* 2003;52(No. RR-1)				
Hepatitis B Vaccines for Hemodialysis-dependent Adults				
Hepatitis B				
Recombivax-HB[2]	40 mcg[5]	1	3	0, 1, and 6
Engerix-B[1]	40 mcg[5]	2.0[4]	4	0, 1, 2, and 6
Source: Adapted from CDC guidelines, *MMWR* 2001;50(No. RR.- 5)				

[1] Manufactured by GlaxoSmithKline Biologicals

[2] Manufactured by Merck & Co., Inc.

[3] Enzyme linked immunosorbent assay (ELISA) units.

[4] Two 1.0 mL doses administered at one site in a 4-dose schedule at 0, 1, 2, and 6 months.

[5] Recommended route/site for administration is the deltoid by intramuscular injection.

Appendix 6a. Contact Investigation - Acute Hepatitis B

Inmate name: **Date of Report:** ___/___/_____

Inmate number: **Facility:** **Date/Facility entry:** ___/___/_____

Date symptom onset: ___/___/_____ **Date BOP entry:** ___/___/_____

Reported by (name and title):

Laboratory Test	Date	Result
IgM anti-HAV		
IgM anti-HBC		
HBsAg		
anti HCV by ☐EIA ☐RNA ☐RIBA		
ALT/AST		

1. **Reported to local health department?** ☐**Yes** ___/___/___ ☐**No** (reason_____)
2. **In the 6 weeks to 6 months prior to illness onset, was patient in a BOP facility?**
   ☐Yes (complete BOP investigation necessary) ☐No (health department to do investigation)
3. **Risk factors** (6 weeks to 6 months prior to illness onset):
   a) Did patient have close contact with a person with confirmed or suspected HBV infection?
   ☐No ☐Yes: ☐sexual partner ☐cell mate ☐dorm mate ☐other:_____
   b) Illicit drug use? ☐Yes ☐No
   c) Sexual partners? ☐Yes (#____) ☐No
   d) Other reported contact with human blood? ☐No
   ☐Yes (when what circumstances:_____)
   e) On dialysis? ☐Yes ☐No
   f) Recent hospitalization ☐No
   ☐Yes (when? where?_____)
   g) *Recent IV infusions or injections received in outpatient setting?* No
   ☐ Yes (When? Where? _____)
   h) Recent dental work No
   ☐ Yes (When? Where? _____)
   i) Recent tattoo ☐Yes ☐ No
   j) Body piercing ☐Yes ☐ No

Appendix 6a. Contact Investigation - Acute Hepatitis B (page 2)

4. Vaccination history:

Vaccinated against hepatitis B? ☐ No

☐Yes When? Dose #1 date_____ Dose #2 date _____ Dose #3 date_____

5. Review prior opportunities for prevention of this case:

Was patient a cell or dormitory mate of a person with acute hepatitis? ☐Yes ☐No

6. Contact evaluation: Consider total anti-HBc testing to determine contacts' susceptibility.

7. Contact management: Inmates in close contact with an inmate diagnosed with acute hepatitis B should be considered for post-exposure prophylaxis.

NOTE: For susceptible inmate contacts with identified or suspected percutaneous or mucosal exposures, administer post-exposure prophylaxis by initiating the first dose of hepatitis B vaccine series IM in the deltoid muscle along with HBIG 0.06 ml/kg body weight IM at a separate site (Give HBIG only if within 7 days of exposure).

NOTE: For susceptible inmate contacts without identified or suspected per cutaneous or mucosa exposures, initiate the first dose of hepatitis B vaccine, but do not give HBIG.

NOTE: Contacts include: injection drug use contacts, sexual contacts, tattoo contacts, and close personal contacts (Establish line listing).

Appendix 6b. Line Listing - Acute Hepatitis B (Limited Official Use)

Suspected percutaneous or mucosal exposure

#	Contact Name	Registration #	Date HBIG given	Date vaccinated

Close contacts (i.e., cellmates, sharing of personal items, etc.) without identified percutaneous / mucosal exposure (i.e., ring vaccination)

#	Contact Name	Registration #	Date vaccine series initiated

Appendix 7.	Management of Hepatitis B Virus Exposures [1]		
Vaccination Status/ Antibody Status	**Treatment Based on Source's HBsAg Status**		
	HBsAg positive	**HBsAg negative**	**Unknown Status**
Unvaccinated	HBIG [2] X 1; Initiate HB vaccine series	Initiate HB vaccine series	Initiate HB vaccine series
Vaccinated known responder (adequate anti-HBs is 10 mIU/ml)	No treatment	No treatment	No treatment
Vaccinated known nonresponder	HBIG X 1 and revaccination series, or HBIG X 2[3]	No treatment unless never revaccinated; then begin a revaccination series	Treat as if source were HBsAg-positive
Vaccinated unknown response status	Test exposed person for anti-HBs: If adequate - no treatment If inadequate - HBIG X 1 plus vaccine booster	No treatment	Test exposed person for anti-HBs: If adequate - no treatment If inadequate - give vaccine booster/recheck titer in 1 - 2 months

[1] Exposure is percutaneous (laceration, needlestick, bite) or permucosal (ocular or mucous-membrane) contact with blood.

[2] HBIG dose is 0.06 mL/kg administered IM at different site than vaccine, preferably < 24 hours after exposure, but no greater than 7 days post- exposure.

[3] Give 1 dose of HBIG and reinitiate vaccine series for nonresponders who have not completed second 3-dose vaccine series; Give HBIG X 2 for nonresponders who have failed second vaccine series.

Adapted from: CDC. Updated U.S. Public Health Service guidelines for the management of occupational exposures to HBV, HCV, and HIV and recommendations for post-exposure prophylaxis. *MMWR* 2001;50(RR-11):1-52

Appendix 8. Step-wise Approach for Evaluating and Treating Chronic Hepatitis C

1. Screen for Hepatitis C Virus Infection

- Risk factors present: if EIA+ or CIA+, then considered infected
- No risk factors: confirm infection if EIA+ or CIA+ with a qualitative HCV RNA test

2. Baseline Evaluation

- Medical history / physical examination.
- Establish duration of infection by history.
- CBC, serum chemistries, INR, anti-HIV, HBsAg
- Evaluate other potential causes of liver disease, as appropriate
- Assess contraindications to interferon and ribavirin prior to liver biopsy or consideration for tx
- Evidence of decompensated cirrhosis → manage without antiviral therapy

3. Review Treatment Contraindications and Considerations

- Mental health assessment to identify suicidal ideation or uncontrolled psychiatric illness
- Assess alcohol use / substance abuse history and counsel on risk reduction. Referrals as appropriate.
- Ensure that sentence length is sufficient to complete a course of treatment.

4. Determine Genotype

5. Confirm chronic HCV infection prior to liver biopsy

- Detect HCV RNA by a quantitative assay, if negative reevaluate with qualitative HCV RNA assay.

6. Liver Biopsy

- Offer liver biopsy to most inmates, regardless of genotype (see text)
- If liver biopsy is normal or shows minimal fibrosis → monitor / re-biopsy in 2-5 years
- If portal or bridging fibrosis and moderate inflammation and necrosis → consider antiviral therapy

7. Drug Therapy

- **HCV Genotype 2 or 3:**
  - *Option 1*
    - Treat with pegylated interferon / ribavirin for 4 weeks; then check quantitative HCV RNA
    - If viral load has decreased by 2 logs or is undetectable, complete total of 12 weeks of treatment
  - *Option 2*
    - Treat with pegylated interferon / ribavirin for 12 weeks; then check quantitative HCV RNA
    - Complete 24 weeks of treatment if HCV RNA is undetectable or ≥ 2 log decrease from baseline
    - Discontinue treatment (nonresponder) if HCV RNA has not shown a ≥ 2 log decrease at 12 weeks
- **HCV Genotype 1, 4, 5, 6, or HIV co-infected:**
  - Treat with pegylated interferon / ribavirin combination therapy
  - Check quantitative HCV RNA after 12 weeks
  - If viral levels have not decreased by 2 logs (10^2) at 12 weeks - discontinue therapy
  - Otherwise continue therapy for 48 weeks

8. Monitor post-treatment

- Measure qualitative HCV RNA assay at completion of treatment
- Measure qualitative HCV RNA 6 months after completion of effective therapy
- Referral to drug education / treatment program if appropriate and not previously completed.

Abbreviations: EIA - enzyme immunoassay; CIA - chemiluminescence immunoassay; RIBA - recombinant immunoblot assay; NAT - nucleic acid test; ALT - alanine aminotransferase; ULN - upper limits of normal.

Appendix 9. *Contraindications for Interferon / Ribavirin Therapy**

Interferon (standard and pegylated)

Absolute Contraindications

- Decompensated cirrhosis
- Potential life-threatening extrahepatic disease such as refractory AIDS, malignancy, severe COPD, or angina
- Uncontrolled autoimmune disorders
- Poorly controlled diabetes
- Solid organ transplantation (kidney, heart, or lung)
- Untreated or uncontrolled hyperthyroidism
- Active suicidal ideation or other neuropsychiatric condition that is poorly controlled
- Ongoing alcohol or injection drug usage - refer for evaluation

Relative Contraindications

- Bone marrow dysfunction - neutropenia/thrombocytopenia
- Hepatitis B co-infection
- HIV infection that is poorly controlled with HAART
- History of recent alcohol abuse or injection drug usage - refer for evaluation

Ribavirin

Absolute Contraindications

- Pregnancy - due to risk of fetal malformations and fetal death; pregnancy test required

  NOTE: *women of childbearing potential AND men must use two forms of effective contraception during treatment and during the six-months post-treatment*
- Men whose female partners are pregnant
- Hemoglobinopathies (sickle cell anemia and homozygous thalassemia), hemolytic anemias or other severe anemias
- Ischemic cardiovascular disease or cerebrovascular disease
- Renal insufficiency - creatinine clearance < 50 ml/min or serum creatinine > 2.0 mg/dL

*Refer to drug manufacturers' warnings in addition to highlighted contraindications

Appendix 10a. Antiviral Medications for Chronic Hepatis C - Interferon Preparations

Medications	Baseline Tests	Monitoring	Adverse Reactions	Comments
Pegylated Interferon alfa-2b (PEG-Intron®) For dosing see *Appendix 10c*	▸ history / physical ▸ ALT / AST ▸ bilirubin ▸ albumin ▸ alkaline phos ▸ PT / INR ▸ CBC (diff & plts) ▸ chemistry panel ▸ creatinine / BUN ▸ thyroid function studies ▸ ferritin / ANA ▸ anti HIV ▸ HBsAg ▸ liver biopsy ▸ HCV genotype	▸ Clinician evaluation every week x 1 month, then monthly. ▸ ALT at weeks 1, 2, 4 and 8-12 weeks thereafter ▸ CBC (with diff and plts), at weeks 1,2,4, and 4-8 weeks thereafter. ▸ TSH every 3 months. ▸ Renal and liver function studies periodically; and whenever clinically warranted. ▸ Screen for depression ▸ Psychologic / psychiatric evaluations as clinically needed.	▸ fever ▸ fatigue ▸ myalgia ▸ psychiatric (rage, confusion, depression, suicide) ▸ bone marrow suppression ▸ thyroid dysfunction ▸ renal failure	Pegylated *interferon in* combination with ribavirin is the recommended treatment regimen for chronic hepatitis C for most patients. Patients with compensated cirrhosis and HIV co-infection may have more severe adverse effects: *monitor* hematologic parameters closely.
Pegylated Interferon alfa-2a (PEGASYS®) For dosing see *Appendix 10c*				

Appendix 10b. Antiviral Medications for Chronic Hepatis C - Ribavirin Preparations

Medications	Baseline Tests	Monitoring	Adverse Reactions	Comments
Ribavirin with interferon (REBETOL®) **Ribavirin [1,2] with pegylated interferon** **For dosing see *Appendix 10c***	▸ CBC (with diff and plts) ▸ *See* baseline tests for interferon since ribavirin always given in combination with interferon preparation. ▸ Pregnancy test for all female inmates.	Ongoing monitoring of hemoglobin and hematocrit for evidence of hemolytic anemia which often occurs between 1 and 4 weeks after initiating therapy. **Note:** *Women of childbearing potential AND men must use two forms of birth control during treatment AND during the 6 months after antiviral therapy is completed.* Consider monthly pregnancy tests for female inmates at risk of pregnancy, e.g., community access.	Hemolysis: expect 5-10% decrease in hematocrit. Note: patients with cirrhosis may have more severe anemia. Note: anemia may precipitate angina, dyspnea, fatigue **Teratogenic** - counsel women AND men regarding the risk of birth defects and the necessity of birth control before, during, & 6 mos. after treatment. Counseling is particularly important for inmates awaiting release and after treatment is completed.	Ribavirin capsules should be taken with food. Ribavirin should be administered on pill line to ensure compliance and increase efficacy. The optimal dose of ribavirin depends on HCV genotype, i.e., higher doses are required for genotype 1. Ribavirin should not be used in patients with a serum creatinine of > 2 mg/dL, or a creatinine clearance of < 50 ml/min.

[1]COPEGUS® and REBETOL®, are formulated as tablets and capsules respectively; and are considered to be bioequivalent by the FDA. Generic formulations are also available.

[2]In clinical studies pegylated interferon alfa-2a was administered with COPEGUS ® and pegylated interferon alfa-2b was administered with REBETOL®.

Appendix 10c. Antiviral Medications for Chronic Hepatitis C
Drug Doses & Administration

Generic (Trade Name)	Recommended Dose
Peginterferon Regimens (plus Ribavirin)	
Peginterferon alfa-2a (Pegasys®) or **Peginterferon alfa-2b (Peg-Intron®)** plus **Ribavirin (Rebetol®; Copegus®)**	▸ 180 µg SQ once weekly regardless of weight ▸ 1.5 µg/kg SQ once weekly ▸ Genotype 1, 4, 5, 6: < 75 kg: 400 mg PO every morning. and 600 mg every evening ≥ 75 kg: 600 mg BID ▸ Genotype 2 and 3: 400 mg PO BID
Regimens Used in Certain Clinical Circumstances	
Peginterferon alfa-2a (Pegasys®) as monotherapy	▸ 180 µg SQ once weekly regardless of weight
Peginterferon alfa-2b (Peg-Intron®) as monotherapy	▸ 1.0 µg/kg SQ once weekly
Interferon alfa-2b plus ribavirin (Rebetron®)	▸ Interferon alfa-2b 3 mU three times weekly SQ **and** Ribavirin: < 75 kg: 400 mg PO every morning. and 600 mg every evening ≥ 75 kg: 600 mg BID
Peginterferon alfa-2a (Pegasys®) in hemodialysis	▸ 135 µg SQ once weekly

From: Strader DB, Wright T, Thomas DL, Seeff LB.; Practice Guidelines Committee, American Association for the Study of Liver Diseases (AASLD). Diagnosis Management and Treatment of Hepatitis C. *Hepatology* 2004; 39:1147-1171.

Appendix 10d. Antiviral Medications for Chronic Hepatitis C - Dosage Adjustments

Medication	Parameter	Adjustment
Interferons	WBC < 1500/mm^3 neutrophil count < 750/mm^3 platelet ct < 80,000/mm^3	▸ reduce dose by 50%
Ribavirin	hemoglobin < 10 g/dL	▸ reduce dose to 200 mg per day
Ribavirin and Interferons	hemoglobin < 8.5 g/dL WBC < 1000/mm^3 neutrophil count < 500/mm^3 platelet count < 50,000/mm^3 platelet count < 25,000/mm^3	▸ discontinue ▸ discontinue ▸ discontinue ▸ Peginterferon alfa-2a ⇒ discontinue ▸ Peginterferon alfa-2b ⇒ discontinue
History of Cardiac Disease (CHF, previous MI, angina, or known CAD by angiography)		
Ribavirin	2 g/dL drop in hemoglobin during any four week period of treatment.	reduce dose to 200 mg AM, 400 mg q HS
Interferon		reduce dose by 50%
Ribavirin and Interferons	hemoglobin < 12 g/dL after 4 weeks at reduced dose above	discontinue
History of Renal Disease		
Ribavirin	creatinine clearance < 50 ml/min or serum creatinine > 2.0 mg/dL	contraindicated; discontinue

Appendix 11a. Contact Investigation - Acute Hepatitis C

Inmate name: Date of Report: ___/___/_____

Inmate number: Facility: Date/Facility entry: ___/___/_____

Date symptom onset: ___/___/_____ Date BOP entry: ___/___/_____

Reported by (name and title):

Laboratory Test	Date	Result
IgM anti-HAV		
IgM anti-HBC		
HBsAg		
anti HCV by ☐EIA ☐RNA ☐RIBA		
HCV RNA ☐qualitative ☐quantitative		
ALT/AST		

1. **Reported to local health department?** ☐Yes ___/___/___ ☐No (reason_____)
2. **In the 2 weeks to 6 months prior to illness onset, was patient in a BOP facility?**
   ☐Yes (complete BOP investigation necessary) ☐No (health department to do investigation)
3. **Risk factors** (2 weeks to 6 months prior to illness onset):
   a) Did patient have close contact with a person with confirmed or suspected HCV infection?
   ☐No☐Yes: ☐sexual partner ☐cell mate ☐dorm mate ☐other:_____
   b) Injection drug use? ☐Yes ☐No
   c) Sexual partners? ☐Yes (#____) ☐No
   d) Other reported contact with human blood? ☐No
   ☐Yes (when/what circumstances:_____)
   e) On dialysis? ☐Yes: ☐dialysis center notified ☐No
   f) Recent hospitalization ☐No
   ☐Yes (when? where?_____)
   g) Recent IV infusions or injections received *in outpatient setting*? ☐No
   ☐ Yes (When? Where? _____)
   h) Recent dental work ☐No
   ☐ Yes (When? Where? _____)
   i) Recent tattoo ☐Yes ☐ No
   j) Body piercing ☐Yes ☐ No
4. **Prior Prevention Opportunities:**
   Was patient a cell or dorm mate of person with acute hepatitis? ☐Yes ☐ No
5. **Contact notification** (HCV counseling and testing should be offered and line listing completed)

Appendix 11b. Line Listing - Acute Hepatitis C (Limited Official Use)

#	Contact Name	Registration #	Anti HCV status (+ or -)	Counseling and Testing Date

Appendix 12. Resources - Prevention and Treatment of Viral Hepatitis

American Association for the Study of Liver Diseases

https://www.aasld.org/eweb/StartPage.aspx

Centers for Disease Control and Prevention

National Center for Infectious Diseases - Hepatitis Branch

http://www.cdc.gov/ncidod/diseases/hepatitis/

MELD Score Calculator

The MELD score can be calculated by utilizing a calculator provided by United Network for Organ Sharing available at:
http://www.unos.org/resources/MeldPeldCalculator.asp?index=98

National Institutes of Health

National Institute of Diabetes and Digestive Disease

http://www.niddk.nih.gov

National Clinicians' Post-Exposure Prophylaxis Hotline

(888) 448-4911

Veterans Affairs National Hepatitis C Web Site

http://hepatitis.va.gov/